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(54) Title: DIHYDROXYPYRIMIDINE CARBOXAMIDE INHIBITORS OF HIV INTEGRASE

(57) Abstract: 4,5-Dihydroxypyrimidine-6-carboxamides of formula (I); are described as inhibitors of HIV integrase and inhibitors of HIV replication, wherein R¹, R², R³ and R⁴ are defined herein. These compounds are useful in the prevention and treatment of infection by HIV and in the prevention, delay in the onset, and treatment of AIDS. The compounds are employed against HIV infection and AIDS as compounds per se or in the form of pharmaceutically acceptable salts. The compounds and their salts can be employed as ingredients in pharmaceutical compositions, optionally in combination with other antivirals, immunomodulators, antibiotics or vaccines. Methods of preventing, treating or delaying the onset of AIDS and methods of preventing or treating infection by HIV are also described.

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TITLE OF THE INVENTION
DIHYDROXYPYRIMIDINE CARBOXAMIDE INHIBITORS OF HIV
INTEGRASE

5 FIELD OF THE INVENTION

The present invention is directed to 5,6-dihydroxypyrimidine-4-carboxamides and pharmaceutically acceptable salts thereof, their synthesis, and their use as inhibitors of the HIV integrase enzyme. The compounds and pharmaceutically acceptable salts thereof of the present invention are useful for preventing or treating infection by HIV and for treating or delaying the onset of AIDS.

BACKGROUND OF THE INVENTION

A retrovirus designated human immunodeficiency virus (HIV) is the etiological agent of the complex disease that includes progressive destruction of the immune system (acquired immune deficiency syndrome; AIDS) and degeneration of the central and peripheral nervous system. This virus was previously known as LAV, HTLV-III, or ARV. A common feature of retrovirus replication is the insertion by virally-encoded integrase of proviral DNA into the host cell genome, a required step in HIV replication in human T-lymphoid and monocytoid cells. Integration is believed to be mediated by integrase in three steps: assembly of a stable nucleoprotein complex with viral DNA sequences; cleavage of two nucleotides from the 3' termini of the linear proviral DNA; covalent joining of the recessed 3'OH termini of the proviral DNA at a staggered cut made at the host target site. The fourth step in the process, repair synthesis of the resultant gap, may be accomplished by cellular enzymes.

Nucleotide sequencing of HIV shows the presence of a pol gene in one open reading frame [Ratner, L. et al., Nature, 313, 277(1985)]. Amino acid sequence homology provides evidence that the pol sequence encodes reverse transcriptase, integrase and an HIV protease [Toh, H. et al., EMBO J. 4, 1267 (1985); Power, M.D. et al., Science, 231, 1567 (1986); Pearl, L.H. et al., Nature, 329, 351 (1987)]. All three enzymes have been shown to be essential for the replication of HIV.

It is known that some antiviral compounds which act as inhibitors of HIV replication are effective agents in the treatment of AIDS and similar diseases, including reverse transcriptase inhibitors such as azidothymidine (AZT)

and efavirenz and protease inhbitors such as indinavir and nelfinavir. The compounds of this invention are inhibitors of HIV integrase and inhibitors of HIV replication. The inhibition of integrase in vitro and HIV replication in cells is a direct result of inhibiting the strand transfer reaction catalyzed by the recombinant integrase in vitro in HIV infected cells. The particular advantage of the present invention is highly specific inhibition of HIV integrase and HIV replication.

SUMMARY OF THE INVENTION

The present invention is directed to novel dihydroxypyrimidine

carboxamides. These compounds are useful in the inhibition of HIV integrase, the
prevention of infection by HIV, the treatment of infection by HIV and in the
prevention, treatment, and delay in the onset of AIDS, either as compounds or their
pharmaceutically acceptable salts or hydrates (when appropriate), or as
pharmaceutical composition ingredients, whether or not in combination with other

HIV/AIDS antivirals, anti-infectives, immunomodulators, antibiotics or vaccines.

More particularly, the present invention includes a compound of Formula (I):

wherein

20 R¹ is

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(1) -H,

-C₁₋₆ alkyl, which is optionally substituted with one or more substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-C₀₋₆ alkyl-N(RaRb), N(Ra)-C(=O)-C₀₋₆ alkyl-N(RbRc), -SO₂Ra, -N(Ra)SO₂Rb,

		$-N(R^a)C(=O)N(R^bR^c)$, $-N(R^a)C(=O)C(=O)N(R^bR^c)$, or	
		-N(Ra)C(=O)ORb	
	(3)	-O-C ₁₋₆ alkyl, which is optionally substituted with one or more	
		substituents each of which is independently halogen, -OH, -CN,	
5		-O-C ₁₋₆ alkyl, -O-C ₁₋₆ haloalkyl, -C(=O)Ra, -CO ₂ Ra, -SRa,	
		$-S(=O)R^a$, $-N(R^aR^b)$, $-C(=O)-C_{0-6}$ alkyl- $N(R^aR^b)$,	
		$N(R^a)$ -C(=O)-C ₀₋₆ alkyl-N(R ^b R ^c), -SO ₂ R ^a , -N(R ^a)SO ₂ R ^b ,	
		$-SO_2N(R^aR^b)$, or $-N(R^a)-C(R^b)=0$,	
	(4)	-Rk,	
10	(5)	-C ₁₋₆ alkyl-R ^k , wherein the alkyl is optionally substituted with one or	
		more substituents each of which is independently halogen, -OH, -CN, -O-C1-6 alkyl, -O-C1-6 haloalkyl, -N(RaRb), -N(Ra)CO2Rb,	
		-N(Ra)C(=O)-C0-6 alkyl-N(RbRc), or -N(Ra)-C2-6 alkyl-OH with the	
		proviso that the -OH is not attached to the carbon alpha to N(Ra),	
15	(6)	-C ₂₋₅ alkenyl-R ^k ,	
	(7)	-C ₂₋₅ alkynyl-R ^k ,	
	(8)	-C ₀₋₆ alkyl-O-C ₀₋₆ alkyl-R ^k ,	
	(9)	-C ₀₋₆ alkyl-S(O) _n -C ₀₋₆ alkyl- \mathbb{R}^k ,	
	(10)	-O-C ₁₋₆ alkyl-OR ^k ,	
20	(11)	-O-C ₁₋₆ alkyl-O-C ₁₋₆ alkyl-R ^k ,	
	(12)	$-O-C_{1-6}$ alkyl- $S(O)_nR^k$,	
	(13)	$-C_{0-6}$ alkyl-N(R ^a)-R ^k ,	
	(14)	-C ₀₋₆ alkyl-N(R^a)-C ₁₋₆ alkyl- R^k ,	
	(15)	- C_{0-6} alkyl- $N(R^a)$ - C_{1-6} alkyl- OR^k ,	
25	(16)	$-C_{0-6}$ alkyl-C(=0)-R ^k ,	
	(17)	$-C_{0-6}$ alkyl-C(=0)N(Ra)-C ₀₋₆ alkyl-Rk,	
	(18)	$-C_{0-6}$ alkyl-N(Ra)C(=0)-C ₀₋₆ alkyl-R ^k ,	
	(19)	$-C_{0-6}$ alkyl-N(Ra)C(=O)-O-C ₀₋₆ alkyl-R ^k ,	
	(20)	-C ₁₋₆ alkyl which is:	
30		(i) substituted with aryl or -O-aryl, wherein the aryl is optionally	
		substituted with one or more substituents each of which is independently halogen, -OH, -C1-6 alkyl, -C1-6 alkyl-ORa,	
		-C ₁₋₆ haloalkyl, -O-C ₁₋₆ alkyl, -O-C ₁₋₆ haloalkyl,	

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methylenedioxy attached to two adjacent carbon atoms, or aryl,

- substituted with -Rk, -C₁₋₆ alkyl-Rk, -N(Ra)-C(=0)-C₀₋₆ (ii) alkyl-Rk, -C0-6 alkyl-N(Ra)-C0-6 alkyl-Rk, -C0-6 alkyl-O-C0-6 alkyl-Rk, or -C0-6 alkyl-N(Ra)-C(=O)-C0-6 alkyl-Rk; and
- optionally substituted with one or more substituents each of which is independently halogen, -OH, -CN, -O-C1-6 alkyl, -O-C₁₋₆ haloalkyl, or -N(RaRb), or
- -C1-6 alkyl, substituted with -O-C1-6 alkyl, and with a substituent (21) 10 selected from the group consisting of -N(Ra)C(=0)Rk and $-N(Ra)C_{1-6}$ alkyl- R^k ,

R² is -H or -C₁₋₆ alkyl which is optionally substituted with one or more substituents

each of which is independently 15 halogen, (1) -OH, (2) -CN, (3) -O-C1-6 alkyl, (4) -O-C1-6 haloalkyl, 20 (5) (6) $-C(=O)R^a$, (7)-CO2Ra, -SRa, (8) (9) -S(=O)Ra, 25 -N(RaRb), (10)-C(=O)N(RaRb),(11) $-N(R^a)-C(=O)-C_{1-6}$ alkyl $-N(R^bR^c)$, (12)-SO₂Ra, (13)

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- (14) $-N(Ra)SO_2Rb$, -SO2N(RaRb), (15)
- (16)-N(Ra)-C(Rb)=O, -C3-8 cycloalkyl, (17)
- (18) aryl, wherein the aryl is optionally substituted with one or more substituents each of which is independently halogen, -C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl,

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-C0-6 alkyl-N(RaRb), or -C1-6 alkyl substituted with a 5or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S;

wherein the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C1-6 alkyl, oxo, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or

a 5- to 8-membered monocyclic heterocycle which is saturated (19)or unsaturated and contains from 1 to 4 heteroatoms independently selected from N, O and S; wherein the heterocycle is optionally substituted with one or more substituents each of which is independently -C1-6 alkyl, -O-C1-6 alkyl, oxo, phenyl, or naphthyl;

15 R³ is -H or -C₁₋₆ alkyl;

R4 is

(1)

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- C₁₋₆ alkyl which is optionally substituted with one or more (2) substituents each of which is independently halogen, -OH, O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -NO₂, -N(RaRb), -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -SO₂Ra, or -N(Ra)CO₂Rb,
- C₁₋₆ alkyl which is optionally substituted with one or more (3) substituents each of which is independently halogen, -OH, or O-C1-4 alkyl, and which is substituted with 1 or 2 substituents each of which is independently:
 - C3-8 cycloalkyl, (i)
 - aryl, (ii)

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- a fused bicyclic carbocycle consisting of a (iii) benzene ring fused to a C5-7 cycloalkyl,
- a 5- or 6-membered saturated heterocyclic ring (iv) containing from 1 to 4 heteroatoms independently selected from N, O and S,

a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or a 9- or 10-membered fused bicyclic heterocycle (vi) containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein at least one of the rings is aromatic, (4) C2_5 alkynyl optionally substituted with aryl, C3-8 cycloalkyl optionally substituted with aryl, (5) 10 (6) aryl, a fused bicyclic carbocycle consisting of a benzene ring fused (7) to a C5-7 cycloalkyl, a 5- or 6-membered saturated heterocyclic ring containing from (8) 1 to 4 heteroatoms independently selected from N, O and S, a 5- or 6-membered heteroaromatic ring containing from 1 to 4 15 (9) heteroatoms independently selected from N, O and S, or a 9- or 10-membered fused bicyclic heterocycle containing (10)from 1 to 4 heteroatoms independently selected from N, O and S, wherein at least one of the rings is aromatic; 20 wherein each aryl in (3)(ii) or the aryl (4), (5) or (6) or each fused carbocycle in (3)(iii) or the fused carbocycle in (7) is optionally substituted with one or more substituents each of which is independently halogen, -OH, -C1-6 alkyl, -C1-6 alkyl-OR2, -C1-6 25 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, -CN, -NO2, -N(RaRb), -C₁₋₆ alkyl-N(RaRb), -C(=O)N(RaRb), -C(=O)Ra, -CO₂Ra, -C₁₋₆ alkyl-CO2Ra, -OCO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)SO2Rb, -SO₂N(RaRb), -N(Ra)C(=O)Rb, -N(Ra)CO₂Rb, -C₁-6 alkyl-N(Ra)CO2Rb, aryl, -C1-6 alkyl-aryl, -O-aryl, or -C0-6 alkyl-het wherein het is a 5- or 6-membered heteroaromatic ring containing from 30 1 to 4 heteroatoms independently selected from N, O and S, and het is

optionally fused with a benzene ring, and is optionally substituted with one or more substituents each of which is independently -C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ haloalkyl, oxo, or -CO₂R^a;

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each saturated heterocyclic ring in (3)(iv) or the saturated heterocyclic ring in (8) is optionally substituted with one or more substituents each of which is independently halogen, -C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, oxo, aryl, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and

each heteroaromatic ring in (3)(v) or the heteroaromatic ring in (9) or each fused bicyclic heterocycle in (3)(vi) or the fused bicyclic heterocycle in (10) is optionally substituted with one or more substituents each of which is independently halogen, -C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, oxo, aryl, or -C1-6 alkyl-aryl;

or alternatively R³ and R⁴ together with the N to which both are attached form a C₃₋₇ azacycloalkyl which is optionally substituted with one or more substituents each of which is independently -C₁₋₆ alkyl or oxo;

each Ra, Rb, Rc, and Rd is independently -H or -C1-6 alkyl;

Rk is carbocycle or heterocycle, wherein the carbocycle or heterocycle is optionally substituted with one or more substituents each of which is independently

- (1) halogen,
- (2) -OH,
- (3) -CN,
 (4) -C1-6 alkyl, which is optionally substituted with one or more substituents each of which is independently halogen,
 -OH, -CN, -O-C1-6 alkyl, -O-C1-6 haloalkyl,
 -C(=O)Ra, -CO2Ra, -SRa, -S(=O)Ra, -N(RaRb),
 -C(=O)-(CH2)0-2N(RaRb),
 N(Ra)-C(=O)-(CH2)0-2N(RbRc), -SO2Ra,
 -N(Ra)SO2Rb, -SO2N(RaRb), or -N(Ra)-C(Rb)=O,

-O-C₁-6 alkyl, which is optionally substituted with one or more substituents each of which is independently halogen,
 -OH, -CN, -O-C₁-6 alkyl, -O-C₁-6 haloalkyl,

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-C(=O)Ra, -CO_2Ra, -SRa, -S(=O)Ra, -N(RaRb),
                                      -C(=O)-(CH_2)_{0-2}N(RaRb),
                                      N(R^a)-C(=O)-(CH_2)_{0-2}N(R^bR^c), -SO<sub>2</sub>R<sup>a</sup>,
                                      -N(R^a)SO_2R^b, -SO_2N(R^aR^b), or -N(R^a)-C(R^b)=O,
                      (6)
                              -NO<sub>2</sub>,
                      (7)
                              oxo,
                              ethylenedioxy, spiro substituted on a ring carbon in a saturated
                      (8)
                              ring of Rk,
                              -C(=O)R^a,
                      (9)
                      (10)
                              -CO<sub>2</sub>Ra,
10
                              -SRa,
                      (11)
                      (12)
                              -S(=O)Ra,
                              -N(RaRb),
                      (13)
                              -C(=O)N(RaRb),
                      (14)
15
                              -C(=O)-C_{1-6} alkyl-N(RaRb),
                      (15)
                              -N(Ra)C(=O)Rb
                      (16)
                      (17)
                              -SO<sub>2</sub>Ra,
                      (18)
                              -SO<sub>2</sub>N(RaRb),
                      (19)
                              -N(R^a)SO_2R^b,
                      (20)
                              -Rm,
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                              -C<sub>1-6</sub> alkyl-Rm, wherein the alkyl is optionally substituted with
                      (21)
                                      one or more substituents each of which is independently
                                    halogen, -OH, -CN, -C1-6 haloalkyl, -O-C1-6 alkyl,
                                      -O-C<sub>1-6</sub> haloalkyl, -C(=O)Ra, -CO<sub>2</sub>Ra, -SRa,
                                      -S(=O)Ra, -N(RaRb), -N(Ra)CO2Rb, -SO2Ra,
25
                                      -N(Ra)SO_2Rb, -SO_2N(RaRb), or -N(Ra)-C(Rb)=O,
                              -C0-6 alkyl-N(Ra)-C0-6 alkyl-Rm,
                      (22)
                              -C0-6 alkyl-O-C0-6 alkyl-Rm,
                      (23)
                              -C0-6 alkyl-S-C0-6 alkyl-Rm,
                      (24)
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                              -C_{0-6} alkyl-C(=0)-C<sub>0-6</sub> alkyl-R<sup>m</sup>,
                      (25)
                              -C(=O)-O-C0-6 alkyl-Rm,
                      (26)
                              -C(=O)N(R^a)-C_{0-6} alkyl-Rm,
                     (27)
                              -N(Ra)C(=O)-Rm,
                      (28)
                              -N(Ra)C(=O)-C<sub>1-6</sub> alkyl-Rm, wherein the alkyl is optionally
                      (29)
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substituted with one or more substituents each of which is independently halogen, -OH, -CN, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, -C(=O)Ra, -CO2Ra, -SRa, -S(=O)Ra, -N(RaRb), -N(Ra)CO2Rb, -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), or -N(Ra)-C(Rb)=O,

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- (30) $-N(R^a)-C(=O)-N(R^b)-C_{0-6}$ alkyl- R^m ,
- (31) -N(Ra)-C(=0)-O-C₀₋₆ alkyl-Rm, or
- (32) -N(Ra)-C(=O)-N(Rb)-SO2-C0-6 alkyl-Rm;
- carbocycle in Rk is (i) a C3 to C8 monocyclic, saturated or unsaturated ring, (ii) a C7 to C12 bicyclic ring system, or (iii) a C11 to C16 tricyclic ring system, wherein each ring in (ii) or (iii) is independent of or fused to the other ring or rings and each ring is saturated or unsaturated;
- heterocycle in Rk is (i) a 4- to 8-membered, saturated or unsaturated monocyclic ring, (ii) a 7- to 12-membered bicyclic ring system, or (iii) an 11 to 16-membered tricyclic ring system; wherein each ring in (ii) or (iii) is independent of or fused to or bridged with or spiro to the other ring or rings and each ring is saturated or unsaturated; the monocyclic ring, bicyclic ring system, or tricyclic ring system contains from 1 to 6
 heteroatoms selected from N, O and S and a balance of carbon atoms; and wherein any one or more of the nitrogen and sulfur heteroatoms is optionally be oxidized, and any one or more of the nitrogen heteroatoms is optionally quaternized;
 - each Rm is independently C₃₋₈ cycloalkyl; aryl; a 5- to 8-membered monocyclic
 heterocycle which is saturated or unsaturated and contains from 1 to 4 heteroatoms
 independently selected from N, O and S; or a 9- to 10-membered bicyclic heterocycle
 which is saturated or unsaturated and contains from 1 to 4 heteroatoms independently
 which is saturated or unsaturated and contains from 1 to 4 heteroatoms independently
 selected from N, O and S; wherein any one or more of the nitrogen and sulfur
 heteroatoms in the monocyclic or bicyclic heterocycle is optionally oxidized and any
 one or more of the nitrogen heteroatoms is optionally quaternized; and wherein

the cycloalkyl or the aryl is optionally substituted with one or more substituents each of which is independently halogen, -C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, -N(RaRb), aryl, or -C1-6 alkyl-aryl; and

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the monocyclic or bicyclic heterocycle is optionally substituted with one or more substituents each of which is independently halogen, -C1-6 alkyl optionally substituted with -O-C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, oxo, aryl, -C1-6 alkyl-aryl, -C(=O)-aryl, -CO2-aryl, -CO2-C1-6 alkyl-aryl, a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and

each n is independently an integer equal to zero, 1 or 2;

or a pharmaceutically acceptable salt thereof.

An embodiment of the present invention is a compound of Formula (I) as originally defined above except that: (I) in the definition of R^1 , R^1 is one of the groups (1) to (20), all of which are as defined above except that (2) of R^1 is -C1-6 alkyl, which is optionally substituted with one or more substituents each of which is independently halogen, -OH, -CN, -O-C1-6 alkyl, -O-C1-6 haloalkyl, -C(=O)Ra, -CO2Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-C0-6 alkyl-N(RaRb), N(Ra)-C(=O)-C0-6 alkyl-N(RbRc), -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb),

20 $-N(R^a)-C(=O)R^b$, or

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The present invention also includes pharmaceutical compositions containing a compound of the present invention and methods of preparing such pharmaceutical compositions. The present invention further includes methods of treating AIDS, methods of delaying the onset of AIDS, methods of preventing AIDS, methods of preventing infection by HIV, and methods of treating infection by HIV.

Other embodiments, aspects and features of the present invention are either further described in or will be apparent from the ensuing description, examples and appended claims.

30 DETAILED DESCRIPTION OF THE INVENTION

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The present invention includes the dihydroxypyrimidine carboxamides of Formula (I) above. These compounds and pharmaceutically acceptable salts thereof are HIV integrase inhibitors.

An embodiment of the present invention is a compound of Formula (I) exactly as defined above, except that in the definition of Rk, Rk is optionally substituted with one or more substituents each of which is independently one of the substituents (1) to (19), and is optionally mono-substituted with one of the substituents (20) to (32).

Another embodiment of the present invention is a compound of Formula (I), wherein R1 is: 10

- -C₁₋₆ alkyl, which is optionally substituted with from 1 to 5 (1) (2) substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O) \mathbb{R}^a , -CO₂ \mathbb{R}^a , -SR^a, $-S(=O)R^a$, $-N(R^aR^b)$, $-C(=O)-(CH_2)O-2N(R^aR^b)$, $N(R^a)$ -C(=O)-(CH₂)₀₋₂ $N(R^bR^c)$, -SO₂ R^a , -N(R^a)SO₂ R^b ,

 $-SO_2N(R^aR^b), -N(R^a)-C(=O)R^b,$

-N(Ra)C(=O)N(RbRc), -N(Ra)C(=O)C(=O)N(RbRc), or -N(Ra)C(=O)ORb,

(3) 20

- -C₁₋₄ alkyl-R^k, wherein the alkyl is optionally substituted with 1 or 2 (4) substituents each of which is independently halogen, -OH, -CN, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -N(RaRb), or -N(Ra)-(CH2)2-4-OH,
- $-O-(CH_2)_{0-3}-R^k$, (5)
- -C₁₋₄ alkyl-O-(CH₂)0-3- \mathbb{R}^k , (6) 25
 - $-(CH_2)_{0-3}-S(O)_{n}-(CH_2)_{0-3}-R^k$ (7)
 - -O-(CH₂)₁-3-OR^k, (8)
 - $-O-(CH_2)_{1-3}-O-(CH_2)_{1-3}-R^k$, (9)
 - $-O-(CH_2)_{1-3}-S(O)_nR^k$, (10)
- $-(CH_2)_{0-3}-N(R^a)-R^k$, (11)30
 - $-(CH_2)_{0-3}-N(R^a)-(CH_2)_{1-3}-R^k$ (12)
 - $-(CH_2)_{0-3}-N(R^a)-(CH_2)_{1-3}-OR^k$, (13)

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- (14) $-(CH_2)_{0-3}-C(=O)-R^k$,
- (15) $-(CH_2)_{0-3}-C(=O)N(R^a)-(CH_2)_{0-3}-R^k$,
- (16) $-(CH_2)_{0-3}-N(R_a)C(=O)-(CH_2)_{0-3}-R^k$,
- (17) $-(CH_2)_{0-3}-N(R^a)C(=O)-O-(CH_2)_{0-3}-R^k$,
- 5 (18) -C₁₋₆ alkyl which is:
 - (i) substituted with aryl or -O-aryl, wherein the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -OH, -C1-4 alkyl, -C1-4 alkyl-ORa, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl,

methylenedioxy attached to two adjacent carbon atoms, or aryl;

- $\label{eq:continuous} \begin{array}{ll} \text{(ii)} & \text{substituted with -Rk, -(CH_2)_{1-3}-Rk,} \\ & -N(R^a)-C(=O)-(CH_2)_{0-3}-R^k$, -(CH_2)_{0-3}-N(R^a)-(CH_2)_{0-3}-R^k$,} \\ & \text{or -(CH_2)_{0-3}-O-(CH_2)_{0-3}-Rk, or} \\ & -(CH_2)_{0-3}-N(R^a)-C(=O)-(CH_2)_{0-3}-R^k$; and} \end{array}$
- optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -CN, -O-C1-4 alkyl, -O-C1-4 haloalkyl, or -N(RaRb),
- (19) $-C(CH_3)_2N(R^a)C(=O)OCH_2R^k$,
- (20) -C(CH₃)₂N(Ra)CH₂Rk,
- (21) $-C(CH_3)_2N(R^a)C(=O)R^k$, or
 - (22) $-C(R^b)(N(R^a)C(=O)R^k)(CH_2OR^c),$
 - (23) $-C(R^b)(N(R^a)(CH_2)-R^k)(CH_2OR^c)$,

and all other variables are as originally defined above;

25 or a pharmaceutically acceptable salt thereof.

Still another embodiment of the present invention is a compound of Formula (I) as defined in the immediately preceding embodiment, except that R1 is one of the groups (1) to (18), wherein (2) of R1 is C₁₋₆ alkyl, which is optionally substituted with from 1 to 5 substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-(CH₂)0-2N(RaRb), N(Ra)-C(=O)-(CH₂)0-2N(RbRc),

-SO₂Ra, -N(Ra)SO₂Rb, -SO₂N(RaRb), -N(Ra)-C(=O)Rb, or

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Another embodiment of the present invention is a compound of Formula (I), wherein R1 is:

-H, (1)

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-C₁₋₄ alkyl, which is optionally substituted with from 1 to 3 (2)substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O) \mathbb{R}^a , -CO₂ \mathbb{R}^a , -SR a , $-S(=O)R^{a}, -N(R^{a}R^{b}), -C(=O)-(CH_{2})_{0}-2N(R^{a}R^{b}),$ $N(R^a)$ -C(=O)-(CH₂)₀-2 $N(R^bR^c)$, -SO₂ R^a , -N(R^a)SO₂ R^b ,

 $-SO_2N(R^aR^b)$, $-N(R^a)-C(=O)R^b$,

- $-N(R^a)C(=O)N(R^bR^c)$, $-N(R^a)C(=O)C(=O)N(R^bR^c)$, or 10. $-N(R^a)C(=O)OR^b$,
 - -Rk, (3)
 - -CH(CH3)-Rk, (4)
 - -(CH2)1-4-Rk, wherein the -(CH2)1-4- moiety is optionally substituted (5) with one of -N(RaRb) or -N(Ra)-(CH2)2-OH,
 - -(CH₂)₁₋₂-O-(CH₂)₀₋₁-R^k, (6)
 - $-(CH_2)_{1-2}-S(O)_n-(CH_2)_{0-1}-R^k$ (7)
 - -O-(CH2)1-2-ORk, (8)
 - $-O-(CH_2)_{1-2}-O-(CH_2)_{1-2}-R^k$, (9)
- $-O-(CH_2)_{1-2}-S(O)_nR^k$, (10)20
 - $-(CH_2)_{1-2}-N(R^a)-R^k$, (11)
 - $-(CH_2)_{1-2}-N(R^a)-(CH_2)_{1-3}-R^k$ (12)
 - $-(CH_2)_{1-2}-N(R^a)-(CH_2)_{1-3}-OR^k$ (13)
 - $-(CH_2)_{0-2}-C(=O)-R^k$, (14)
- $-C(=O)N(R^a)-(CH_2)_{1-2}-R^k$, (15)25
 - $-(CH_2)_{0-2}-C(=O)N(R^a)-(CH_2)_{0-2}-R^k$ (16)
 - $-(CH_2)_{1-2}-N(R^a)C(=O)-(CH_2)_{0-1}-R^k,\\$ (17)
 - $-(CH_2)_{1-2}-N(R^a)C(=O)-O-(CH_2)_{0-1}-R^k$ (18)
 - -C₁₋₄ alkyl which is: (19)
- substituted with aryl or -O-aryl wherein the aryl is optionally (i) 30 substituted with from 1 to 3 substituents each of which is independently fluoro, chloro, -C1-4 alkyl, -C1-4 fluoroalkyl,

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-O-C₁₋₄ alkyl, -O-C₁₋₄ fluoroalkyl, methylenedioxy attached to two adjacent carbon atoms, or phenyl;

- (ii) substituted with $-R^k$, $-(CH_2)_{1-3}-R^k$, $-N(R^a)-C(=O)-(CH_2)_{0-3}-R^k$, $-N(R^a)-(CH_2)_{1-3}-R^k$, $-O-(CH_2)_{1-2}-R^k$, or $-N(R^a)-C(=O)-(CH_2)_{0-2}-R^k$; and
- (iii) optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, or -N(R^aR^b),
- (20) -C(CH₃)₂N(R_a)C(=O)OCH₂R_k,
- 10 (21) $-C(CH_3)_2N(R^a)CH_2R^k$,
 - (22) $-C(CH_3)_2N(R^a)C(=O)R^k$,
 - (23) $-C(R^b)(N(R^a)C(=O)R^k)(CH_2OR^c)$, or
 - (24) $-C(R^b)(N(R^a)(CH_2)-R^k)(CH_2OR^c);$
- and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

In an aspect of this embodiment, R¹ is

(1) -H,

-C₁₋₄ alkyl, which is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)R^a, -CO₂R^a, -SR^a, -S(=O)R^a, -N(R^aR^b), -C(=O)-(CH₂)0-2N(R^aR^b), N(R^a)-C(=O)-(CH₂)0-2N(R^bR^c), -SO₂R^a, -N(R^a)SO₂R^b,

25 $-SO_2N(R^aR^b)$, $-N(R^a)-C(=O)R^b$, or

- (3) -R k ,
- (4) $-CH(CH_3)-R^k$,
- (5) -(CH₂)₁₋₄-Rk, wherein the -(CH₂)₁₋₄- moiety is optionally substituted with one of -N(RaRb) or -N(Ra)-(CH₂)₂-OH,
- 30 (6) -(CH₂)₁₋₂-O-(CH₂)₀₋₁-R^k,
 - (7) $-(CH_2)_{1-2}-S(O)_{n}-(CH_2)_{0-1}-R^k$,
 - (8) $-O-(CH_2)_{1-2}-OR^k$,

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	(9)	-O-(CH ₂) ₁₋₂ -O-(CH ₂) ₁₋₂ -R ^k ,
	(10)	-O-(CH ₂) ₁₋₂ -S(O) _n R ^k ,
	•	-(CH ₂) ₁ -2-N(R ^a)-R ^k ,
	(11)	-(CH ₂) ₁₋₂ -N(R ^a)-(CH ₂) ₁₋₃ -R ^k ,
	(12)	-(CH ₂) ₁₋₂ -N(R ^a)-(CH ₂) ₁₋₃ -OR ^k ,
5	(13)	-(CH ₂) ₀ -2-C(=O)-R ^k ,
	(14)	$-C(=O)N(R^{a})-(CH_{2})1-2-R^{k}$
	(15)	$-(CH_2)_{0-2}-C(=O)N(R^a)-(CH_2)_{0-2}-R^k$
	(16)	-(CH2)0-2-C(=0)N(Ra)-(CH2)0-2-A
	(17)	-(CH ₂) ₁₋₂ -N(R ^a)C(=0)-(CH ₂) ₀₋₁ -R ^k ,
10	(18)	$-(CH_2)_{1-2}-N(R^a)C(=O)-O-(CH_2)_{0-1}-R^k$, or
	(19)	-C ₁ -4 alkyl which is:
	, ,	conditioned with aryl or -O-aryl wherein the aryl is optionally
		having a with from 1 to 3 substituents each of which is
		independently fluoro, chloro, -C1-4 alkyl, -C1-4 muoroatkyl,
		-O-C ₁₋₄ alkyl, -O-C ₁₋₄ fluoroalkyl, methylenedioxy attached
15		to two adjacent carbon atoms, or phenyl;
		Dk (CH2)1 3-Rk
		(ii) substituted with -kk, -(CH2/1-3 kl, -N(Ra)-(CH2)1-3-Rk, -N(Ra
		-N(Ra)-C(=O)-(CH2)0-3-R-1, -N(Ra)-C(=O)-(CH2)0-2-Rk; and -O-(CH2)1-2-Rk, or -N(Ra)-C(=O)-(CH2)0-2-Rk; and
		-O-(CH2)1-2-RK, or -N(Ra)-C(-O)-(CH2)0-2
20		(iii) optionally substituted with from 1 to 4 substituents each of
20		which is independently halogen, -OH, -CN, -O-C1-4 with
		-O-C1-4 haloalkyl, or -N(RaRb).

Another embodiment of the present invention is a compound of

25 Formula (I), wherein

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Rk is C₃₋₈ cycloalkyl; aryl selected from phenyl and naphthyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S;

wherein the cycloalkyl, aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 4 substituents each of which is independently

	to 4 substitu	ents eaci	1 Of which is independently
		(1)	halogen,
5		(2)	-OH,
		(3)	-CN,
	,	(4)	-C ₁₋₄ haloalkyl,
		(5)	-C ₁₋₄ alkyl, which is optionally substituted with from 1 to 3
10			substituents each of which is independently -OH, -CN, -O-C ₁₋₄ alkyl, -O-C ₁₋₄ haloalkyl, -C(=0)R ^a , -CO ₂ R ^a , -SR ^a , -S(=0)R ^a , -N(R ^a R ^b), -C(=0)-(CH ₂) ₀₋₂ N(R ^a R ^b), N(R ^a)-C(=0)-(CH ₂) ₀₋₂ N(R ^b R ^c), -SO ₂ R ^a , -N(R ^a)SO ₂ R ^b , -SO ₂ N(R ^a R ^b), or -N(R ^a)-C(R ^b)=O,
:		(6)	-O-C1-4 haloalkyl
15		(7)	-O-C ₁₋₄ alkyl, which is optionally substituted with from 1 to 3
			substituents each of which is independently -OH, -CN, -O-C ₁₋₆ alkyl, -O-C ₁₋₆ haloalkyl, -C(=0)R ^a , -CO ₂ R ^a , -S(=0)R ^a , -N(R ^a R ^b), -C(=0)-(CH ₂) ₀₋₂ N(R ^a R ^b), N(R ^a)-C(=0)-(CH ₂) ₀₋₂ N(R ^b R ^c), -SO ₂ R ^a ,
20			$-N(Ra)SO_2R^b$, $-SO_2N(RaR^b)$, or $-N(Ra)-C(R^b)=O$,
20		(8)	-NO2,
		(9)	
		(10)	oxo, -C(=O)Ra,
	•	(11)	-C(20)R ² ,
25		(12)	-SRa,
23		(12)	-S(=O)Ra,
		(14)	-N(RaRb),
		(15)	-C(=O)N(RaRb),
		(16)	-C(=O)-C1-6 alkyl-N(RaRb),
30	•	(17)	$-N(R^a)C(=O)R^b$,
50		(18)	-SO ₂ Ra,
	•	(18)	-SO ₂ N(RaRb),
		(19)	-N(Ra)SO ₂ Rb,
	•	(20)	-Rm,
35		(21)	-CH(CH ₃)-R ^m ,

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-(CH2)1-4-Rm,
                   (22)
                           -(CH2)0-2-N(Ra)-(CH2)0-2-Rm,
                   (23)
                           -(CH_2)_{0-2}-O-(CH_2)_{0-2}-R^m
                    (24)
                           -(CH2)0-2-S-(CH2)0-2-Rm,
                    (25)
                           -(CH_2)_{0-2}-C(=O)-(CH_2)_{0-2}-R^m
                    (26)
5
                           -C(=O)-O-(CH2)0-2-Rm,
                    (27)
                           -C(=O)N(Ra)-Rm,
                    (28)
                           -N(Ra)C(=O)-Rm
                    (29)
                           -N(R^a)C(=O)-(CH_2)1-3-R^m, wherein the -(CH_2)1-3- moiety is
                    (30)
                                   optionally substituted with one of -N(RaRb),
10
                                   -N(R^a)CO_2R^b, -SO_2R^a, -N(R^a)SO_2R^b, -SO_2N(R^aR^b), \\
                                   or -N(R^a)-C(R^b)=O,
                           -N(R^a)-C(=O)-N(R^b)-(CH_2)_{1-2}-R^m,
                    (31)
                            -N(R^a)-C(=O)-O-(CH_2)_{1-2}-R^m, or
                    (32)
                            -N(R^a)-C(=O)-N(R^b)SO_2-R^m;
                    (33)
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and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

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In an aspect of this embodiment, Rk (i.e., the cycloalkyl, aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle) is optionally substituted with from 1 to 4 substituents each of which is independently one of the substituents (1) to (19), and is optionally mono-substituted with one of the substituents (20) to (33). In a feature of this aspect, Rk is optionally substituted with from 1 to 4 substituents each of which is independently one of the substituents (1) to (19), and is mono-substituted with one of the substituents (20) to (33).

In another aspect of this embodiment, each Rm is independently C5-7 cycloalkyl; aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene

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ring fused to a 5- or 6-membered, saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms selected from N, O and S; wherein

the cycloalkyl or the aryl is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁-4 alkyl, -C₁-4 haloalkyl, -O-C₁-4 alkyl, -O-C₁-4 haloalkyl, -N(RaRb), phenyl, or -(CH₂)₁-2-phenyl;

the saturated heterocyclic ring is optionally substituted with from 1 to 4 substituents each of which is independently -C1-4 alkyl optionally substituted with -O-C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, oxo, phenyl, -(CH2)1-2-phenyl, -C(=O)-phenyl, -CO2-phenyl, -CO2-(CH2)1-2-phenyl, a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and

the heteroaromatic ring or the bicyclic heterocycle is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, oxo, phenyl, or -(CH₂)₁₋₂-phenyl.

Another embodiment of the present invention is a compound of 20 Formula (I), wherein Rk is cycloalkyl selected from cyclopropyl, cyclopentyl and cyclohexyl; aryl selected from phenyl and naphthyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring selected from pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, pyranyl, tetrahydrofuranyl, imidazolidinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, 25 oxazolidinyl, isooxazolidinyl, and pyrazolidinyl; a 5- or 6-membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxopiperidinyl, oxazolyl, isooxazolyl, oxadiazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl; or a bicyclic heterocycle selected from indolyl, indolinyl, tetrahydroquinolinyl, quinolinyl, 30 tetrahydroisoquinolinyl, isoquinolinyl, 1,4-dioxa-8-azaspiro[4.5]dec-8-yl, azabicyclo[2.2.1]hept-1-yl, azabicyclo[2.1.1]hex-1-yl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo-1,4-dioxinyl, and benzo-1,3-dioxolyl;

35 and all other variables are as originally defined above;

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or a pharmaceutically acceptable salt thereof.

In an aspect of this embodiment, Rk is as just defined except that it excludes cyclopropyl, pyranyl, oxopiperidinyl, 1,4-dioxa-8-azaspiro[4.5]decyl, azabicyclo[2.2.1]heptyl, and azabicyclo[2.1.1]hexyl.

In another aspect of this embodiment, the cycloalkyl, aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

	opuonary bassass	
	(1)	fluoro,
10	(2)	chloro,
	(3)	bromo,
	(4)	-CF ₃ ,
	(5)	-C ₁₋₄ alkyl, which is optionally substituted with 1 or 2
15	•	substituents each of which is independently -OH, -CN, -O-C1-4 alkyl, -OCF3, -N(RaRb), -C(=O)N(RaRb), or
		N(Ra)-C(=O)-(CH2)0-2N(RbRc),
	(6)	OCE-

- (6) -OCF₃,
- (7) -O-C₁₋₄ alkyl
- (8) -NO₂,
- 20 (9) oxo,

- (10) $-C(=O)R^a$,
 - (11) -CO₂Ra,
 - (12) -SRa,
 - (13) $-S(=O)R^a$,
- 25 (14) -N(RaRb),
 - (15) -C(=O)N(RaRb),
 - (16) $-C(=O)-(CH_2)_{1-2}-N(R^aR^b)$,
 - (17) $-N(R^a)C(=O)R^b$,
 - (18) -SO₂Ra,
- 30 (19) -R^m,
 - (20) -CH(CH₃)-Rm,
 - (21) -CH₂-Rm,
 - (22) $-(CH_2)_{0-2}-N(R^a)-(CH_2)_{0-2}-R^m$,
 - (23) -O-(CH₂)₁₋₂-Rm,
- 35 (24) -(CH₂)₀₋₁-S-(CH₂)₀₋₂-R^m,

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(25) -(CH ₂) ₀₋₁ -C(=O)-(CH ₂) ₀₋	-2-R ^m ,
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- (26) $-(CH_2)_{0-1}-C(=O)-O-(CH_2)_{0-2}-R^m$,
- (27) $-C(=O)N(R^a)-R^m$,
- (28) $-N(R^a)C(=O)-R^m$,
- (29) -N(Ra)C(=0)-(CH2)1-2-Rm, wherein the -(CH2)1-2- moiety is optionally substituted with -N(RaRb),
 - (30) $-N(R^a)-C(=O)-N(R^b)-(CH_2)_{1-2}-R^m$,
 - (31) $-N(Ra)-C(=O)-O-(CH_2)_{1-2}-Rm$,
 - (32) $-N(R^a)-C(=O)-N(R^b)SO_2-R^m$, or

10 (33) -OH.

In another aspect of this embodiment, the substituents are selected from substituents (1) to (32) just defined.

In another aspect of this aspect, the cycloalkyl, aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently one of the substituents (1) to (18) as just defined in the preceding aspect, and is optionally mono-substituted with one of the substituents (19) to (32) as just defined in the preceding aspect.

In still another aspect of this embodiment, each R^m is independently aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperidinyl, piperazinyl, thiazolidinyl, and morpholinyl; or a 5- or 6-membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiadiazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl,

25 furanyl, and pyridazinyl; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(R^aR^b);

the saturated heterocyclic ring is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, oxo, phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-CH₂-phenyl; and

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, oxo, phenyl, or -(CH2)1-2-phenyl.

In an aspect of this embodiment, the 5- or 6-membered saturated heterocyclic ring is selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperidinyl, and morpholinyl.

Another embodiment of the present invention is a compound of Formula (I), wherein R² is -H or -C₁₋₆ alkyl which is optionally substituted with one of:

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- (1) -N(RaRb),
- phenyl which is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, or -C₀₋₆ alkyl-N(R^aR^b), or
- 15 (3) a 5- or 6-membered saturated monocyclic heterocycle which contains from 1 to 4 heteroatoms independently selected from N, O and S; wherein the heterocycle is optionally substituted with from 1 to 4 substituents each of which is independently -C1-6 alkyl, -O-C1-6 alkyl, oxo, or phenyl;
- 20 and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

In an aspect of the preceding embodiment, R2 is

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- (1) -H
- (2) -C₁₋₄ alkyl,
- (3) $-(CH_2)_{1-3}-N(R^aR^b)$,
- (4) -(CH2)1-3-phenyl, wherein the phenyl is optionally substituted

with from 1 to 3 substituents each of which is independently fluoro, chloro, bromo,

- 30 -C₁₋₄ alkyl, -C₁₋₄ fluoroalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ fluoroalkyl, or -(CH₂)₁₋₃-N(R^aR^b); or
 - (5) -(CH2)1-3R^t, wherein R^t is a 6-membered saturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S.

Other embodiments of the present invention include a compound wherein \mathbb{R}^2 is -H or methyl; or \mathbb{R}^2 is -H; and all other variables are as originally defined above; or a pharmaceutically acceptable salt thereof.

Another embodiment of the present invention is a compound of Formula (I), wherein R³ is -H or -C₁-4 alkyl;

and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

In an aspect of this embodiment, \mathbb{R}^3 is -H or methyl. In another aspect of this embodiment, \mathbb{R}^3 is -H.

Another embodiment of the present invention is a compound of Formula (I), wherein \mathbb{R}^4 is

(1) C_{1-4} alkyl,

(2) C₁₋₄ alkyl substituted with from 1 to 3 substituents each of which is independently -OH, O-C₁₋₄ alkyl, or -O-C₁₋₄ haloalkyl,

(3) C₁₋₄ alkyl which is substituted with an aryl or with two aryls which are the same or different, and is optionally substituted with -OH,

(4) C₁₋₄ alkyl substituted with one of:

- (i) C5-7 cycloalkyl,
- (ii) a fused bicyclic carbocycle consisting of a benzene ring fused to a C5-7 cycloalkyl,
- (iii) a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S,
- (iv) a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or

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	•	
		(v) a 9- or 10-membered fused bicyclic heterocycle
		containing from 1 to 4 heteroatoms
		independently selected from N, O and S,
		wherein at least one of the rings is aromatic;
5	(5)	C ₂₋₄ alkynyl optionally substituted with aryl,
	(6)	C ₃₋₇ cycloalkyl optionally substituted with aryl,
	(7)	aryl,
	(8)	a fused bicyclic carbocycle consisting of a benzene ring fused
	``	to a C5-7 cycloalkyl,
10	(9)	a 5- or 6-membered saturated heterocyclic ring containing from
	•	1 to 4 heteroatoms independently selected from N, O and S,
	(10)	a 5- or 6-membered heteroaromatic ring containing from 1 to 4
	•	heteroatoms independently selected from N, O and S, or
	(11)	a 9- or 10-membered fused bicyclic heterocycle containing
15	` '	from 1 to 4 heteroatoms independently selected from N, O and
15		S, wherein at least one of the rings is aromatic;
	where	ein
		each aryl in (3) or the aryl in (5), (6) or (7) or the fused
		carbocycle in (4)(ii) or (8) is optionally substituted with from 1
20		to 4 substituents each of which is independently halogen, -OH,
20		-C ₁ -4 alkyl, -C ₁ -4 alkyl-OR ^a , -C ₁ -4 haloalkyl, -O-C ₁ -4 alkyl,
		-O-C ₁₋₄ haloalkyl, -CN, -NO ₂ , -N(RaRb), -C ₁₋₄
		alkyl-N(RaRb), -C(=O)N(RaRb), -C(=O)Ra, -CO ₂ Ra, -C ₁ -4
		alkyl-CO2Ra, -OCO2Ra, -SRa, -S(=O)Ra, -SO2Ra,
25		$-N(R^a)SO_2R^b$, $-SO_2N(R^aR^b)$, $-N(R^a)C(=O)R^b$,
		-N(Ra)CO ₂ Rb, -C ₁₋₄ alkyl-N(Ra)CO ₂ Rb, phenyl, -C ₁₋₄
		alkyl-phenyl, -O-phenyl, or -(CH2)0-2-het wherein het is a 5-
		or 6-membered heteroaromatic ring containing from 1 to 4
		heteroatoms independently selected from N, O and S, and het i
30		optionally fused with a benzene ring, and is optionally
		substituted with 1 or 2 substituents each of which is
		independently -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl,
		-O-C ₁₋₄ haloalkyl, or -CO ₂ Ra;
		the saturated heterocyclic ring in (4)(iii) or (9) is
35		optionally substituted with from 1 to 4 substituents each of

which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, oxo, phenyl, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and the heteroaromatic ring in (4)(iv) or (10) or the fused bicyclic

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heterocycle in (4)(v) or (11) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁-4 alkyl, -C₁-4 haloalkyl, -O-C₁-4 alkyl, -O-C₁-4 haloalkyl, oxo, or phenyl;

and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

Another embodiment of the present invention is a compound of

15 Formula (I), wherein R4 is:

(1) C₁₋₃ alkyl substituted with 1 or 2 phenyls, and is optionally substituted with an -OH,

- (2) C₁₋₄ alkyl substituted with one of:
 - (i) cyclohexyl,

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- (ii) naphthyl,
- (iii) a fused bicyclic carbocycle selected from

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(iv) a saturated heterocyclic ring containing from zero to 1 oxygen atoms and from 1 to 3 nitrogen atoms,

 (v) a 5- or 6-membered heteroaromatic ring containing from zero to 1 heteroatoms selected from O and S and from 1 to 3 nitrogen atoms, or

(vi) a fused bicyclic heterocycle selected from

(3) $--(CH_2)_{1-2}$ $C \equiv C - R^u$ wherein R^u is H or phenyl,

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- (4) C₃₋₆ cycloalkyl optionally substituted with phenyl,
- (5) phenyl or naphthyl,
- (6) a fused bicyclic carbocycle selected from

$$z^1$$
 z^1
 z^1
 z^1
 z^1
 z^1

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- (7) a saturated heterocyclic ring containing from zero to 1 oxygen atoms and from 1 to 3 nitrogen atoms,
- (8) a 5- or 6-membered heteroaromatic ring containing from zero to 1 heteroatoms selected from O and S and from 1 to 3 nitrogen atoms, or

15 (9)

wherein Z1 is -H or -OH;

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each phenyl in (1) or the phenyl in (3) or (4) or (5) or the naphthyl in (2)(ii) or (5) is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, bromo, chloro, -OH, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, -CN, -NO₂,

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-(CH₂)₁₋₂-N(RaRb), -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -SO₂Ra, -N(Ra)SO₂Rb, -SO₂N(RaRb), or -N(Ra)CO₂Rb; and is additionally and optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -O-phenyl, or -(CH₂)₀₋₂-het wherein het is thiadiazolyl or indolyl, and het is optionally substituted with -C₁₋₄ alkyl, -CF₃, -O-C₁₋₆ alkyl, -OCF₃, or -CO₂Ra;

the saturated heterocyclic ring in (2)(iv) or (7) is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁_4 alkyl, -CF₃, -O-C₁_4 alkyl, -OCF₃, oxo; and is additionally and optionally mono-substituted with phenyl or a heteroaromatic ring selected from pyridyl, pyrimidinyl, and pyrazinyl; and

the heteroaromatic ring in (2)(v) or (8) is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or oxo; and is additionally and optionally monosubstituted with phenyl;

and all other variables are as originally defined above;

20 or a pharmaceutically acceptable salt thereof.

 $\label{eq:Another embodiment} Another embodiment of the present invention is a compound of Formula (I), wherein <math>\mathbb{R}^4$ is:

25 wherein

Q is

- (1) ethynyl optionally substituted with aryl,
- (2) C5-7 cycloalkyl,
- 30 (3) aryl,

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	(4)	a fused bicyclic carbocycle consisting of a benzene ring fused to a C5-7 cycloalkyl,
	(5)	a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S,
5	(6)	a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or
	(7)	a 9- or 10-membered fused bicyclic heterocycle containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein at least one of the rings is aromatic;
10	wher	
10	WIICI	aryl in (1) or (3) or the fused carbocycle in (4) is optionally
		substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -C1-4 alkyl, -C1-4 alkyl-ORa, -C1-4
		haloalkyl, -O-C1 4 alkyl, -O-C1-4 haloalkyl, -CN, -NO2, -N(Rako),
15		$C_{1.4.4}$ alkyl-N(RaRb), -C(=0)N(RaRb), -C(=0)Ra, -CO ₂ Ra, -C1-4
13		alkyl-CO2Ra, -OCO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)SO2Rb,
		-SO ₂ N(RaRb), -N(Ra)C(=O)Rb, -N(Ra)CO ₂ Rb, -C ₁ -4
		alkyl-N(Ra)CO2Rb, phenyl, -C1_4 alkyl-phenyl, -O-phenyl, or
		-(CH2)0-2-het wherein het is a 5- or 6-membered heteroaromatic ring
		containing from 1 to 4 heteroatoms independently selected from N, O
20		and S, and het is optionally fused with a benzene ring, and is optionally substituted with -C ₁ -4 alkyl, -C ₁ -4 haloalkyl, -O-C ₁ -4 alkyl, -O-C ₁ -4
		haloalkyl, or -CO ₂ Ra;
		the saturated heterocyclic ring in (5) is optionally substituted
25		with from 1 to 4 substituents each of which is independently halogen, -C1_4 alkyl, -C1_4 haloalkyl, -O-C1_4 alkyl, -O-C1_4 haloalkyl, oxo,
	•	phenyl, or a 5- or 6-membered heteroaromatic ring containing from 1
		to 4 heteroatoms independently selected from N, O and S; and
		the heteroaromatic ring in (6) or the fused bicyclic heterocycle
30		in (7) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C ₁₋₄ alkyl, -C ₁₋₄ haloalkyl, -O-C ₁₋₄
		alkyl, -O-C ₁₋₄ haloalkyl, oxo, or phenyl;
		-

R⁵ is H, methyl, or CH₂OH, with the proviso that when R⁵ is CH₂OH, then Q is aryl; and

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p is an integer equal to zero, 1 or 2;

and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

In an aspect of the preceding embodiment, Q is

- (1) —C=C-R^u wherein R^u is H or phenyl,
- 10 (2) phenyl or naphthyl,
 - (3) cyclopentyl or cyclohexyl,
 - (4) a fused bicyclic carbocycle selected from the group consisting of indanyl, tetrahydronaphthalenyl, and benzocycloheptyl,
 - (5) a saturated heterocyclic ring selected from the group consisting of tetrahydrofuranyl, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, and pyrazolidinyl,
 - (6) a heteroaromatic ring selected from the group consisting of thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, oxadiazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl, or
 - (7) a fused bicyclic heterocycle selected from the group consisting of benzothiophenyl, indolyl, pyridoimidazolyl, indazolyl, 2,3-dihydrobenzo-1,4-dioxinyl, dihydrobenzofuranyl, benzo-1,3-dioxolyl, quinolinyl, and isoquinolinyl;

wherein

the phenyl in (1) or the phenyl or naphthyl in (2) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -CN, -NO2, -C1-4 alkyl-N(RaRb), -C(=O)Ra, -CO2Ra, -C1-4 alkyl-CO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), -N(Ra)CO2Rb, -C1-4 alkyl-N(Ra)CO2Rb, phenyl, -(CH2)1-2-phenyl, -O-phenyl, or -(CH2)0-2-het wherein het is pyrrolyl, pyrazolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isothiazolyl, isooxazolyl, pyridyl, pyrazinyl,

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thiadiazolyl or indolyl, and het is optionally substituted with -C1-4 alkyl, -CF3, -O-C1-6 alkyl, -OCF3, oxo, or -CO $_2$ Ra;

the fused carbocycle in (4) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -C1-4 alkyl-N(RaRb), -C(=O)Ra, -CO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)CO2Rb, phenyl, -(CH2)1-2-phenyl, or -O-phenyl;

the saturated heterocyclic ring in (5) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, oxo, phenyl, pyridyl, pyrazinyl, or pyrimidinyl; and

the heteroaromatic ring in (6) or the fused bicyclic heterocycle in (7) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, oxo, or phenyl.

In another aspect of the preceding embodiment, Q is phenyl, which is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, bromo, chloro, -OH, -C1-4 alkyl, -C1-4 fluoroalkyl, -O-C1-4 alkyl, -O-C1-4 fluoroalkyl, -CN, -SRa, -(CH2)1-2-N(RaRb), -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), -(CH2)0-2-CO2Ra*, -(CH2)0-2-N(Ra)CO2Rb*, -NO2, or phenyl;

each Ra is independently H, methyl, or ethyl;

25 each Rb is independently H, methyl, or ethyl; and

each R^{a*} and R^{b*} is independently H or -C₁₋₄ alkyl.

In another aspect of the preceding embodiment, the phenyl substituents are independently selected from the group consisting of fluoro, bromo, chloro, -OH, -C1-4 alkyl, -C1-4 fluoroalkyl, -O-C1-4 alkyl, -O-C1-4 fluoroalkyl, -CN, -(CH2)1-2-N(RaRb), -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), -(CH2)0-2-CO2Ra*, -(CH2)0-2-N(Ra)CO2Rb*, -NO2, and phenyl.

In still another aspect of the preceding embodiment, Q is phenyl which is optionally substituted with from 1 to 3 substituents, each of which is independently

-F, -Br, -Cl, -OH, -C₁₋₄ alkyl, -C₁₋₄ fluoroalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ fluoroalkyl, -CN, -SRa or -SO₂Ra. In still another aspect of the preceding embodiment, Q is phenyl which is optionally substituted with from 1 to 3 substituents, each of which is independently -F, -Br, -Cl, -OH, -C₁₋₄ alkyl, -C₁₋₄ fluoroalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ fluoroalkyl, -CN, or -SO₂Ra.

In still another aspect of the preceding embodiment, Q is p-fluorophenyl or 2,3-dimethoxyphenyl. In still another aspect of the preceding embodiment, Q is p-fluorophenyl.

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In yet another aspect of the preceding embodiment, and also a feature of each of the preceding aspects thereof, R⁵ is H and p is zero.

A class of compounds of the present invention includes any compound of Formula (I), wherein

R1 is -Rk;

Rk is a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms independently selected from N, O and S;

wherein the heteroaromatic ring is optionally substituted with from 1 to 3 substituents each of which is independently

- (1) halogen,
- -C₁₋₆ alkyl, which is optionally substituted with from 1 to 5 substituents each of which is independently halogen,
 -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)R^a, -CO₂R^a,
 -SR^a, -S(=O)R^a, -N(R^aR^b), -C(=O)-(CH₂)₀₋₂N(R^aR^b),
 N(R^a)-C(=O)-(CH₂)₀₋₂N(R^bR^c), -SO₂R^a,
 -N(R^a)SO₂R^b, -SO₂N(R^aR^b), or -N(R^a)-C(R^b)=O,

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- (3) -NO₂,
- (4) oxo,
- (5) $-C(=0)R^a$,
- (6) -CO₂Ra,
- (7) -C(=O)N(RaRb),

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	(8)	$-C(=O)-C_{1-4}$ alkyl- $N(R^{a}R^{b})$,
	(9)	-Rm,
	(10)	-C ₁₋₆ alkyl-R ^m , wherein the alkyl is optionally substituted with
		from 1 to 5 substituents each of which is independently
5		halogen, -OH, -CN, -C1-4 haloalkyl, -O-C1-4 alkyl,
		-O-C ₁₋₄ haloalkyl, -C(=O)R ^a , -CO ₂ R ^a , -SR ^a ,
		$-S(=O)R^a$, $-N(R^aR^b)$, $-N(R^a)CO_2R^b$, $-SO_2R^a$,
		$-N(R^a)SO_2R^b$, $-SO_2N(R^aR^b)$, or $-N(R^a)-C(R^b)=O$,
	(11)	$-C_{0-4}$ alkyl-N(R ^a)-C ₀₋₄ alkyl-R ^m ,
10	(12)	-C ₀₋₄ alkyl-O-C ₀₋₄ alkyl-R ^m ,
,	(13)	-C ₀₋₄ alkyl-S-C ₀₋₄ alkyl-R ^m ,
	(14)	$-C_{0-4}$ alkyl-C(=0)-C ₀₋₄ alkyl-R ^m ,
	(15)	$-C(=O)-O-C_0-4$ alkyl- R^m ,
	(16)	$-C(=O)N(R^a)-C_0-4$ alkyl- R^m ,
15	(17)	$-N(R^a)C(=O)-R^m$
	(18)	-N(Ra)C(=0)-C1-6 alkyl-Rm, wherein the alkyl is optionally
		substituted with from 1 to 5 substituents each of which
		is independently halogen, -OH, -CN, -C1-4 haloalkyl,
	•	-O-C ₁₋₄ alkyl, -O-C ₁₋₄ haloalkyl, -C(=O)R ^a , -CO ₂ R ^a ,
20		-SRa, -S(=O)Ra, -N(RaRb), -N(Ra)CO2Rb, -SO2Ra,
		$-N(R^a)SO_2R^b$, $-SO_2N(R^aR^b)$, or $-N(R^a)-C(R^b)=O$,
	(19)	$-N(R^a)-C(=O)-N(R^b)-C_{0-4}$ alkyl- R^m ,
	(20)	$-N(R^a)-C(=0)-O-C_{0-4}$ alkyl- R^m , or
	(21)	-N(Ra)-C(=O)-N(Rb)SO2-C0-4 alkyl-Rm;
25		1 1 14 1 2 2 5 2 7 6
	wherein each Rm is	independently aryl selected from phenyl and naphthyl or a 5- or 6-
		omatic ring containing from 1 to 3 heteroatoms independently
	selected from N, O	and S; wherein
	the a	ryl is optionally substituted with from 1 to 3 substituents each of
30	which is ind	ependently halogen, -C ₁₋₄ alkyl, -CF ₃ , -O-C ₁₋₄ alkyl, -OCF ₃ , or

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl or oxo; and

-N(RaRb); and

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each Ra and Rb is independently -H or -C1-4 alkyl;

and all other variables are as originally defined above;

or a pharmaeutically acceptable salt thereof.

A sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (I) exactly as defined in the class, except that in the definition of R^k , R^k is optionally substituted with from 1 to 3 substituents each of which is independently one of the substituents (1) to (8), and is optionally mono-substituted with one of the substituents (9) to (21).

Another sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (I), wherein \mathbb{R}^1 is:

R6a is:

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> wherein X1 is a single bond connecting the carbonyl carbon to the carbon substituted with X2, -O-, or -NH-;

 X^2 is -H, -NH₂, or -N(H)CO₂R^a;

Yl is -H, halo or -C1-4 alkyl; and

r is an integer equal to zero, 1 or 2; and

R6b is -H or -NO2; and

R7 is -H or -C1-4 alkyl;

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and all other variables are as defined in the class;

or a pharmaceutically acceptable salt thereof.

In a feature of this sub-class, R6a and R6b are both -H; and 15

R7 is -H or -CH3.

Another class of compounds of the present invention includes any compound of Formula (I), wherein 20

R1 is -Rk;

Rk is phenyl which is optionally substituted with from 1 to 3 substituents each of which is independently: 25

- (1) halogen,
- -C₁₋₆ alkyl, which is optionally substituted with from 1 to 5 (2)substituents each of which is independently halogen, -OH, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -C(=O) \mathbb{R}^a , $-CO_2R^a$, $-SR^a$, $-S(=O)R^a$, $-N(R^aR^b)$, $-C(=O)-(CH_2)_{0-2}N(R^aR^b),$ $N(R^a)-C(=0)-(CH_2)_{0-2}N(R^bR^c)$, -SO₂R^a, $-N(R^a)SO_2R^b$, $-SO_2N(R^aR^b)$, or $-N(R^a)-C(R^b)=O$,

-NO2, (3)

		(4)	-C(=O)Ra,
		(5)	-CO ₂ Ra,
		(6)	-C(=O)N(RaRb),
•		(7)	$-C(=O)-C_{1-4}$ alkyl-N(RaRb),
5		(8)	-R ^m ,
	•	(9)	-C ₁₋₆ alkyl-Rm, wherein the alkyl is optionally substituted with
			from 1 to 5 substituents each of which is independently
			halogen, -OH, -CN, -C1-4 haloalkyl, -O-C1-4 alkyl,
			-O-C ₁₋₄ haloalkyl, -C(=O)Ra, -CO ₂ Ra, -SRa,
10			-S(=O)Ra, -N(RaRb), -N(Ra)CO2Rb, -SO2Ra,
			$-N(Ra)SO_2Rb$, $-SO_2N(RaRb)$, or $-N(Ra)-C(Rb)=O$,
	•	(10)	-C ₀₋₄ alkyl-N(R ^a)-C ₀₋₄ alkyl-R ^m ,
	•	(11)	-C ₀₋₄ alkyl-O-C ₀₋₄ alkyl-R ^m ,
		(12)	-C ₀₋₄ alkyl-S-C ₀₋₄ alkyl-R ^m ,
15		(13)	-C ₀₋₄ alkyl-C(=0)-C ₀₋₄ alkyl-R ^m ,
		(14)	-C(=O)-O-C ₀₋₄ alkyl-R ^m ,
		(15)	$-C(=O)N(R^a)-C_{0-4}$ alkyl- R^m ,
		(16)	-N(Ra)C(=O)-Rm
		(17)	-N(Ra)C(=0)-C ₁₋₆ alkyl-Rm, wherein the alkyl is optionally
20			substituted with from 1 to 5 substituents each of which
			is independently halogen, -OH, -CN, -C1-4 haloalkyl,
			-O-C ₁₋₄ alkyl, -O-C ₁₋₄ haloalkyl, -C(=O) R^a , -CO ₂ R^a ,
			-SRa, -S(=O)Ra, -N(RaRb), -N(Ra)CO ₂ Rb, -SO ₂ Ra,
			$-N(Ra)SO_2Rb$, $-SO_2N(RaRb)$, or $-N(Ra)-C(Rb)=O$,
25		(18)	$-N(R^a)-C(=O)-N(R^b)-C_{0-4}$ alkyl- R^m ,
		(19)	$-N(R^a)-C(=O)-O-C_{0-4}$ alkyl- R^m , or
		(20)	$-N(R^a)-C(=O)-N(R^b)SO_2-C_{0-4}$ alkyl- R^m ;

wherein each Rm is independently aryl selected from phenyl and naphthyl; a 5- or 6membered saturated heterocyclic ring containing from 1 to 3 heteroatoms
independently selected from N, O and S; or a 5- or 6-membered heteroaromatic ring
containing from 1 to 3 heteroatoms independently selected from N, O and S; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(R^aR^b);

the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C₁₋₄ alkyl or oxo, and is additionally optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-(CH₂)₁₋₂-phenyl; and

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently -C1_4 alkyl or oxo;

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and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

15 A sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (I) exactly as defined in the class, except that in the definition of Rk, Rk is optionally substituted with from 1 to 3 substituents each of which is independently one of the substituents (1) to (8), and is optionally mono-substituted with one of the substituents (9) to (20).

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Another sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (I), wherein R^{1} is phenyl which is mono-substituted (e.g., para-substituted) with one of:

(1) fluoro, chloro, or bromo,

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- -C₁₋₄ alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C₁₋₄ alkyl, -OCF₃, -C(=O)R^a, -CO₂R^a, -SR^a, -N(R^aR^b), or -C(=O)N(R^aR^b),
- (3) $-NO_2$,

- (4) $-C_{1-4}$ alkyl- R^{m} ,
- (5) $-O-(CH_2)_{1-2}-R^m$,
- (6) $-(CH_2)_{0-2}-S-(CH_2)_{0-2}-R^m$,
- (7) $-N(R^a)C(=0)-R^m$,
- (8) $-N(R^a)C(=O)-(CH_2)_{1-2}-R^m$, wherein the $(CH_2)_{1-2}$ moiety is

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optionally mono-substituted with -N(R^aR^b) or -N(R^a)CO₂ R^b , or

(9) $-N(R^a)-C(=O)-N(R^b)-(CH_2)_{1-2}-R^m$;

wherein Rm is aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing 1 or 2 heteroatoms independently selected from N and O; or a 5- or 6-membered heteroaromatic ring containing from 1 or 2 nitrogens; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(RaRb); and

the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C₁₋₄ alkyl or oxo; and is additionally and optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-(CH₂)₁₋₂-phenyl; and

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently -C1-4 alkyl or oxo; and

each Ra and Rb is each independently -H or -C1-4 alkyl;

and all other varaibles are as defined in the class;

or a pharmaceutically acceptable salt thereof.

Another class of compounds of the present invention includes any compound of Formula (I), wherein

R1 is -Rk;

Rk is a 5- or 6-membered saturated heterocyclic ring containing from 0 to 1 oxygen atoms and from 1 to 3 nitrogen atoms or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated heterocyclic ring containing from 0 to 1 oxygen atoms and from 1 to 3 nitrogen atoms;

wherein the saturated heterocyclic ring or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

5	(1) (2)	halogen, -C1-6 alkyl, which is optionally substituted with from 1 to 5 substituents each of which is independently halogen, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -C(=O)Ra, -CO2Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-(CH2)0-2N(RaRb), N(Ra)-C(=O)-(CH2)0-2N(RbRc), -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), or -N(Ra)-C(Rb)=O,
	(3)	-NO ₂ ,
	(4)	oxo,
10	(5)	-C(=O)R ^a ,
	(6)	-CO ₂ Ra,
	(7)	-C(=O)N(RaRb),
	(8)	$-C(=O)-C_1$ 4 alkyl-N(RaRb),
	(9)	-SRa,
15	(10)	-S(=O)Ra,
	(11)	-SO ₂ Ra,
	(12)	-N(RaRb),
	(13)	-Rm,
	(14)	-C1-6 alkyl-Rm, wherein the alkyl is optionally substituted with
20		from 1 to 5 substituents each of which is independently halogen, -OH, -CN, -C ₁₋₄ haloalkyl, -O-C ₁₋₄ alkyl, -O-C ₁₋₄ haloalkyl, -C(=O)R ^a , -CO ₂ R ^a , -SR ^a , -S(=O)R ^a , -N(R ^a R ^b), -N(R ^a)CO ₂ R ^b , -SO ₂ R ^a , -N(R ^a)SO ₂ R ^b , -SO ₂ N(R ^a R ^b), or -N(R ^a)-C(R ^b)=O,
25	(15)	-C ₀₋₄ alkyl-N(R ^a)-C ₀₋₄ alkyl-R ^m ,
	(16)	-C ₀₋₄ alkyl-O-C ₀₋₄ alkyl-R ^m ,
	(17)	-C ₀₋₄ alkyl-S-C ₀₋₄ alkyl-R ^m ,
	(18)	$-C_{0-4}$ alkyl- $C(=0)$ - C_{0-4} alkyl- R^{m} ,
	(19)	$-C(=O)-O-C_{0-4}$ alkyl $-R^{m}$,
30	(20)	$-C(=O)N(R^a)-C_{0-4}$ alkyl- R^m ,
	(21)	
	(22)	-N(Ra)C(=0)-C ₁₋₆ alkyl-Rm, wherein the alkyl is optionally
		substituted with from 1 to 5 substituents each of which is independently halogen, -OH, -CN, -C1-4 haloalkyl,
35		-O- C_{1} -4 alkyl, -O- C_{1} -4 haloalkyl, -C(=O) R^{a} , -CO ₂ R^{a} ,

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-SRa, -S(=O)Ra, -N(RaRb), -N(Ra)CO₂Rb, -SO₂Ra, -N(Ra)SO₂Rb, -SO₂N(RaRb), or -N(Ra)-C(Rb)=O,

- (23) $-N(R^a)-C(=O)-N(R^b)-C_{0-4}$ alkyl- R^m ,
- (24) $-N(R^2)-C(=O)-O-C_{0-4}$ alkyl-Rm, or
- (25) $-N(R^a)-C(=O)-N(R^b)SO_2-C_0-4$ alkyl- R^m ;

wherein each Rm is independently aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; or a 9- to 10-membered bicyclic heterocycle which is saturated or unsaturated and contains from 1 to 3 heteroatoms independently selected from N, O and S; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(RaRb);

the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C₁₋₄ alkyl or oxo, and is additionally optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-(CH₂)₁₋₂-phenyl; and

the heteroaromatic ring or the bicyclic heterocycle is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl or oxo;

and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

A sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (I) exactly as defined in the class, except that in the definition of R^k , R^k is optionally substituted with from 1 to 3 substituents each of which is independently one of the substituents (1) to (12), and is optionally mono-substituted with one of the substituents (13) to (25).

Another sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (I), wherein

R1 is:

R8 is:

10 (1) -H, (2) -C₁₋₄

(2) -C₁₋₄ alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C₁₋₄ alkyl, -OCF₃, -C(=O)R^a, -CO₂R^a, -SR^a, -N(R^aR^b), or

-C(=O)N(RaRb),

15 (3) $-C(=O)R^a$,

(4) $-CO_2R^a$,

(5) $-C(=O)-(CH_2)_{1-2}-N(R^aR^b),$

(6) -SO₂Ra,

(7) $-(CH_2)_{1-2}-R^m$,

20 (8) -(CH₂)₀₋₂-C(=O)-(CH₂)₀₋₂-R^m,

(9) $-C(=O)-O-(CH_2)_{0-2}-R^m$, or

(10) $-C(=O)N(R^a)-(CH_2)0-2-R^m;$

R9 is -H, -C1-4 alkyl, or oxo;

5 R10 is -H, -OH, -C1-4 alkyl, -O-C1-4 alkyl, oxo, or -O-(CH2)1-2-R $^{\rm m}$;

R¹¹ is

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(1) -H,

-C1-4 alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C1-4 alkyl, -OCF3, -C(=O)Ra, -CO2Ra, -SRa, -N(RaRb), or -C(=O)N(RaRb),

- (3) $-C(=O)R^a$,
- (4) -CO₂Ra,
- (5) $-C(=O)-(CH_2)_{1-2}-N(R^aR^b),$
- (6) -SO₂Ra,
- (7) $-(CH_2)_{1-2}-R^m$,
- (8) $-(CH_2)_{0-2}-C(=O)-(CH_2)_{0-2}-Rm$,
- (9) $-C(=O)-O-(CH_2)_{0-2}-R^m$, or

20 (10) $-C(=O)N(R^a)-(CH_2)_{0-2}-R^m$;

with the proviso that when one of R^8 and R^{11} is $-(CH_2)_{1-2}-R^m$, $-(CH_2)_{0-2}-C(=O)-(CH_2)_{0-2}-R^m$, $-C(=O)-O-(CH_2)_{0-2}-R^m$, or $-C(=O)N(R^a)-(CH_2)_{0-2}-R^m$, then the other of R^8 and R^{11} is other than

25 -(CH₂)₁₋₂-R^m, -(CH₂)₀₋₂-C(=O)-(CH₂)₀₋₂-R^m, -C(=O)-O-(CH₂)₀₋₂-R^m, or -C(=O)N(R^a)-(CH₂)₀₋₂-R^m;

Rm is aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing 1 or 2 heteroatoms independently selected from N and O; a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a saturated or unsaturated heterocycle containing from 1 to 3 nitrogen atoms; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(RaRb); and

the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently - C_{1-4} alkyl or oxo; and is additionally and optionally mono-substituted with phenyl, - $(CH_2)_{1-2}$ -phenyl, - $(CG_2)_{1-2}$ -phenyl; and

the heteroaromatic ring or the bicyclic heterocycle is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl or oxo; and

each Ra and Rb is independently -H or -C1-4 alkyl;

and all other variables are as defined in the class;

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or a pharmaceutically acceptable salt thereof.

Another embodiment of the present invention is a compound of Formula (I), wherein

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R² is -H or methyl;

 R^3 is -H;

25 R4 is -CH2-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, -CN, -SRa, or -SO2Ra; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

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and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

In an aspect of this embodiment, R⁴ is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F,

-Cl, -Br, -OH, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, -CN, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl.

Aspects of this embodiment include a compound of Formula (I) in which R¹ is as defined in any of the preceding classes or sub-classes.

Another class of compounds of the present invention includes any compound of Formula (II):

$$\mathbb{R}^{12}$$
 \mathbb{R}^{12}
 \mathbb{R}^{12}

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	•		
•	wherein T is:		
		(1)	-Н,
		(2)	-OH,
		(3)	-C ₁₋₄ haloalkyl,
15		(4)	-C1-3 alkyl, optionally substituted with -OH or -O-C1-4 alkyl,
	•	(5)	-O-C ₁₋₄ haloalkyl,
	•	(6)	-O-C ₁₋₄ alkyl
		(7)	-N(RaRb),
		(8)	-N(R ^a)-(CH ₂) ₂ -OH,
20		(9)	-N(Ra)-CO ₂ Rb,
		(10)	$-N(R^a)-C(=O)-(CH_2)_{1-2}-N(R^aR^b),$
		(11)	-Rk,
	and the second s		•

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(13) -(CH₂)₀₋₂-O-(CH₂)₀₋₂-R^k,

 $-(CH_2)_{1-4}-R^k$,

(12)

(14) $-(CH_2)_{0-2}-N(R^a)-(CH_2)_{0-3}-R^k$, or

(15) $-(CH_2)_{0-2}-N(R^a)-C(=O)-(CH_2)_{0-2}-R^k$;

Rk is aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N,

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O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; wherein

the aryl is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C1-4 alkyl, -C1-4 alkyl-OR a , -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, or -N(R a R b); and

the saturated heterocyclic ring is optionally substituted with from 1 to 4 substituents each of which is independently -C1-4 alkyl; -C1-4 alkyl-ORa; -C1-4 haloalkyl; -O-C1-4 alkyl; -O-C1-4 haloalkyl; -C(=O)Ra; oxo; ethylenedioxy spiro substituted on a ring carbon; phenyl; -CH2-phenyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; -CH2-saturated heterocycle which is a a 5- or 6-membered ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S;

the heteroaromatic ring is optionally substituted with from 1 to 4 substituents each of which is independently -C1-4 alkyl, -C1-4 alkyl-ORa, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, or oxo; and

the bicyclic heterocycle is optionally substituted with from 1 to 4 substituents each of which is independently -C₁₋₄ alkyl or oxo;

R12 is phenyl which is optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, Br, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, methylenedioxy attached to two adjacent carbon atoms, or phenyl;

each Ra and Rb is independently -H or -C1-4 alkyl; and

s is an integer equal to zero, 1, 2, or 3;

and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

A sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (II) exactly as defined in the class, except that s is zero, 1 or 2; and with the proviso that when s is 1 or 2, T is -H.

Another sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (II), wherein

R3 is -H; and

R4 is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, -CN, -SR^a, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

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and all other variables are as defined in the class;

or a pharmaceutically acceptable salt thereof.

In a feature of this sub-class, R⁴ is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, -CN, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

25 Still another class of compounds of the present invention includes any compound of Formula (III):

wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, -CN, -SR^a, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

each Ra is independently -H or -C1-4 alkyl

or a pharmaceutically acceptable salt thereof. In a subclass of this class, Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, -CN, or -SO₂R^a.

Still another class of compounds of the present invention includes any compound of Formula (I), wherein

15 R¹ is

(1) -C₁₋₄ alkyl, which is optionally substituted with 1 to 3 substituents each of which is independently fluoro, chloro, -OH, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-(CH₂)0-2N(RaRb), -N(Ra)-C(=O)-(CH₂)1-2N(RbRc), -SO₂Ra, -N(Ra)SO₂Rb,

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 $-SO_2N(R^aR^b)$, $-N(R^a)-C(R^b)=O$,

-N(Ra)C(=O)N(RbRc), -N(Ra)C(=O)C(=O)N(RbRc), or -N(Ra)C(=O)ORb,

(2) $-(CH_2)_{1-3}-R^k$,

(3) -(CH₂)₁₋₃-O-(CH₂)₀₋₂-R^k,

(4) -(CH₂)₁₋₃-N-(CH₂)₀₋₂-R^k,

(5) $-(CH_2)_{1-3}-N(R^a)C(=O)-(CH_2)_{0-2}-R^k$,

(6) $-(CH_2)_{1-3}-N(R^a)C(=O)-O-(CH_2)_{0-2}-R^k$,

(7) $-(CH_2)_{0-3}-C(=O)N(R^a)-(CH_2)_{0-2}-R^k$,

30 (8) -C(=O)-(CH₂)₀₋₂-R^k,

(9) $-C(CH_3)_2N(R^a)C(=O)OCH_2R^k$,

(10) $-C(CH_3)_2N(R^a)CH_2R^k$,

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- (11) $-C(CH_3)_2N(R^a)C(=O)R^k$, or
- (12) $-C(R^b)(N(R^a)C(=O)R^k)(CH_2OR^c)$,

Rk is aryl selected from phenyl and naphthyl, with the proviso that when R¹ is

-(CH₂)₁₋₃-Rk, then Rk is not phenyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S, with the proviso that the bicyclic heterocycle is not benzo-1,3-dioxolyl;

wherein the aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

- (1) fluoro, chloro, or bromo,
- (2) -OH,
- (3) -CN,
- (4) -CF3,

20 (4) -C₁₋₄ alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C

substituents each of which is independently -OH, -O-C1-4 alkyl, -OCF3, -C(=O)Ra, -CO2Ra, -SRa, or -N(RaRb),

- (5) -OCF3,
- (5) -O-C₁₋₄ alkyl,
- 25 (8) oxo,
 - (9) methylenedioxy attached to two adjacent ring carbon atoms,
 - (10) $-C(=O)R^a$,
 - (11) -CO₂Ra,
 - (12) -SRa,
 - (13) -S(=O)Ra,
 - (14) -N(RaRb),
 - (15) $-(CH_2)_{0-2}-C(=O)N(R^aR^b)$,
 - (16) $-C(=O)-(CH_2)_{1-2}-N(R^aR^b)$, or
 - (17) -SO₂Ra;

and all other variables are as originally defined above;

or a pharmaceutically acceptable salt thereof.

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In a sub-class of this class, R1 is

(1) -C₁-4 alkyl, which is optionally substituted with 1 to 3 substituents each of which is independently fluoro, chloro, -OH, -O-C₁-4 alkyl, -O-C₁-4 haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-(CH₂O₂-2N(RaRb), -C(=O)Ra, -N(RaRb), -C(=O)Ra, -C(=O)

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 $-N(R^{a})-C(=O)-(CH_{2})_{1-2}N(R^{b}R^{c}), -SO_{2}R^{a}, -N(R^{a})SO_{2}R^{b}, \\ NR^{b}$

 $-SO_2N(RaRb)$, -N(Ra)-C(Rb)=O, or

- (2) $-(CH_2)_{1-3}-R^k$,
- (3) $-(CH_2)_{1-3}-O-(CH_2)_{0-2}-R^k$,
- (4) -(CH₂)₁₋₃-N-(CH₂)₀₋₂-R^k,

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- (5) $-(CH_2)_{1-3}-N(R^a)C(=O)-(CH_2)_{0-2}-R^k$,
- (6) $-(CH_2)_{1-3}-N(R^a)C(=O)-O-(CH_2)_{0-2}-R^k$,
- (7) $-(CH_2)_{0-3}-C(=O)N(R^a)-(CH_2)_{0-2}-R^k$, or
- (8) -C(=O)-(CH₂)₀₋₂-R^k.

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A sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (I), wherein

R² is -H; and

R4 is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, -CN, -SR^a, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

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each Ra and Rb is independently -H or -C1-4 alkyl;

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Rk is aryl selected from phenyl and naphthyl, with the proviso that when R1 is -(CH₂)₁₋₃-Rk, then Rk is not phenyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S, with the proviso that the bicyclic heterocycle is not benzo-1,3-dioxolyl;

wherein the aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

- (1) fluoro, chloro, or bromo,
- (2) -OH,
- (2) -OII, (3) -CN,
 - (4) -CF₃,
 - (4) -C₁₋₄ alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C₁₋₄ alkyl, -OCF₃, -C(=O)R^a, -CO₂R^a, -SR^a, or -N(R^aR^b),
- 20 (5) -OCF₃,
 - (5) -O-C₁₋₄ alkyl,
 - (8) oxo,
 - (9) methylenedioxy attached to two adjacent ring carbon atoms,
 - (10) $-C(=O)R^a$,
- 25 (11) -CO₂Ra,
 - (12) -SRa,
 - (13) $-S(=O)R^a$,
 - (14) -N(RaRb),
 - (15) $-(CH_2)_{0-2}-C(=O)N(R^aR^b)$,
 - (16) $-C(=O)-(CH_2)_{1-2}-N(R^aR^b)$, or
 - (17) -SO₂Ra;

and all other variables are as defined in the class;

or a pharmaceutically acceptable salt thereof.

In a feature of this sub-class, R4 is -CH2-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, -CN, or -SO $_2$ Ra; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

Still another class of compounds of the present invention includes any compound of Formula (IV):

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wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, -CN, -SRa, or -SO₂Ra; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

each Ra is independently -H or -C1-4 alkyl

or a pharmaceutically acceptable salt thereof.

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In a sub-class of this class, Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, -CN, or -SO2Ra.

Still another class of compounds of the present invention includes any compound of Formula (V):

wherein

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5 R13 is -H or -C1-6 alkyl;

R14 is -H, -C1-6 alkyl, -C(=O)-C1-6 alkyl, -C(=O)-(CH2)0-2-J, or
-C(=O)-O-(CH2)0-2-J; wherein J is aryl selected from phenyl and naphthyl; a 5- or
6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms
independently selected from N, O and S; or a 5- or 6-membered heteroaromatic ring
containing from 1 to 4 heteroatoms independently selected from N, O and S; and
wherein the aryl is optionally substituted with from 1 to 3 substituents
each of which is independently fluoro, chloro, bromo, -CF3, -C1-4 alkyl,
-OCF3, or -O-C1-4 alkyl; and

wherein the saturated heterocyclic ring or heteroaromatic ring is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, chloro, bromo, -CF3, -C1-4 alkyl, -OCF3, -O-C1-4 alkyl, or oxo;

20 R15 and R16 are each independently -C1-6 alkyl; or alternatively R15 and R16 together with the carbon atom to which they are both attached form C3-8 cycloalkyl; and

Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, -CN, -SR^a, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

each Ra is independently -H or -C1-4 alkyl

or a pharmaceutically acceptable salt thereof.

In a sub-class of this class, Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, -CN, or -SO2Ra; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl.

A sub-class of the preceding class of compounds of the present invention includes any compounds of Formula (V), wherein R^{15} and R^{16} are both methyl; or alternatively R^{15} and R^{16} together with the carbon atom to which they are both attached form cyclohexyl;

and all other variables are as defined in the class;

or a pharmaceutically acceptable salt thereof.

It is to be understood that additional embodiments of the present invention include, but are not limited to, compounds of Formula I wherein each of two or three or more of R¹, R², R³, R⁴, R^a, R^b, R^c, R^d, R^k and R^m is independently defined in accordance with its definition in one of the embodiments or an aspect thereof as set forth above, or in accordance with its definition in one of the foregoing classes set forth above or a sub-class or feature thereof. Any and all possible combinations of these variables in Formula I are additional embodiments within the scope of the present invention.

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An aspect of the present invention is a compound selected from the group consisting of

4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-1-(methylamino)ethyl]pyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylmorpholin-3-yl)pyrimidine-4-carboxamide;

- 2-[1-benzoyl-4-(N,N-dimethylglycyl)piperazin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(1-benzoyl-4-methylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-5 carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpiperidin-2-yl)pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)-1,2,3,4-tetrahydroquinolin-2-yl]pyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[4-methyl-1-(pyridin-2-ylcarbonyl)piperazin-2-yl]pyrimidine-4-carboxamide;
- 15
 N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-4-(pyridin-2-ylcarbonyl)piperazin-2-yl]pyrimidine-4-carboxamide;
- 2-(1-ethylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-20 carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-isopropyl-1-methylpiperazin-2-yl)pyrimidine-4-carboxamide;
- 25 2-[1-(acetylamino)cyclohexyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(morpholin-4-ylacetyl)piperidin-2-yl]pyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(pyrrolidin-1-ylmethyl)pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpyrrolidin-2-yl)pyrimidine-4carboxamide;

2-[1-(N,N-dimethylglycyl)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

- 5 N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[(pyridin-2-lcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
 - 2-[1-(dimethylamino)-2-phenylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
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 2-{1-[(2,4-dimethyl-1,3-thiazol-5-yl)carbonyl]piperidin-2-yl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(3-chlorobenzoyl)-4-methylpiperazin-2-yl]-N-(4-fluorobenzyl)-5,6dihydroxypyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-4-(methylsulfonyl)piperazin-2-yl] pyrimidine-4-carboxamide;
- 20 N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-isopropyl-4-methylpiperazin-2-yl)pyrimidine-4-carboxamide;
 - N-(3-bromo-4-fluorobenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-[1-(dimethylamino)cyclohexyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-[(pyridin-2-30 ylcarbonyl)amino]cyclohexyl}pyrimidine-4-carboxamide;

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2-(4-benzyl-1-methylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

- N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(1-piperidin-1-ylethyl)phenyl]pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(2-methyl-1,2,3,4-tetrahydroisoquinolin-3-yl)pyrimidine-4-carboxamide;
 - N-(2,3-dimethoxybenzyl)-2-[1-(N,N-dimethylglycyl)piperidin-2-yl]-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(anilinocarbonyl)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-[(2S,4R)-1-benzoyl-4-(benzyloxy)pyrrolidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)piperidin-2-yl]pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-(morpholin-4-ylacetyl)-1,2,3,4-20 tetrahydroisoquinolin-3-yl]pyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-phenyl-1-[(pyridin-2-lcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
- 25 2-(1-benzoylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-(1-benzylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
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 2-(1-benzoylpyrrolidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-isonicotinoylpiperidin-2-yl)pyrimidine-4carboxamide;

N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-(1-isonicotinoylpiperidin-2-yl)pyrimidine-4-carboxamide;

- 5 N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(methylsulfonyl)piperidin-2-yl]pyrimidine-4-carboxamide;
 - 2-(1-benzoyl-1,2,3,4-tetrahydroquinolin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
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 2-{1-[(N,N-dimethylglycyl)amino]-2-phenylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(piperidin-1-ylmethyl)phenyl]pyrimidine-4-carboxamide;
 - 2-{4-[(diethylamino)methyl]phenyl}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 20 N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-4-ylmethyl)piperidin-2-yl]pyrimidine-4-carboxamide;
 - 2-(1-benzoylpyrrolidin-2-yl)-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
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 tert-butyl 2-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)morpholine-4-carboxylate;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-3-ylcarbonyl)piperidin-2-30 yl]pyrimidine-4-carboxamide;
 - 2-[2-(N,N-dimethylglycyl)-1,2,3,4-tetrahydroisoquinolin-3-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

- 2-(1-benzoyl-2,3-dihydro-1H-indol-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(2-benzoyl-1,2,3,4-tetrahydroisoquinolin-3-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-(1-amino-2-phenylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(4-benzylmorpholin-3-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-[(1-methyl-1H-imidazol-2-yl)carbonyl]piperidin-2-yl}pyrimidine-4-carboxamide;

- N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(morpholin-4-ylmethyl)phenyl]pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(morpholin-4-ylmethyl)pyrimidine-4-20 carboxamide;
 - N-(4-Fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-{4-[({[(2-chlorophenyl)sulfonyl]amino}carbonyl)amino]thien-3-yl}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4 carboxamide;
 - N^4 -(4-fluorobenzyl)-5,6-dihydroxy- N^2 -(pyridin-2-ylmethyl)pyrimidine-2,4-dicarboxamide;
- 30 2-Benzyl-*N*-(4-fluorobenzyl)-5-hydroxy-6-(2-morpholin-4-ylethoxy)pyrimidine-4-carboxamide;
 - and pharmaceutically acceptable salts thereof.

Another aspect of the present invention is a compound selected from the group consisting of

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpiperidin-2-yl)pyrimidine-4-carboxamide;

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- 2-[1-(dimethylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylmorpholin-3-yl)pyrimidine-4-carboxamide;
 - 2-[(dimethylamino)(phenyl)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-{4-[(diethylamino)methyl]phenyl}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - N-benzyl-5,6-dihydroxy-2-(3-phenylpropyl)pyrimidine-4-carboxamide;
- 20 N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)-1,2,3,4-tetrahydroquinolin-2-yl]pyrimidine-4-carboxamide;
 - and pharmaceutically acceptable salts thereof.
 - Another aspect of the present invention is a compound selected from the group consisting of
- benzyl 1-[4-({[4-fluoro-2-(methylsulfonyl)benzyl]amino}carbonyl)-5,6-30 dihydroxypyrimidin-2-yl]-1-methylethylcarbamate;
 - 2-(1-amino-1-methylethyl)-N-[4-fluoro-2-(methylsulfonyl)benzyl]-5,6-dihydroxypyrimidine-4-carboxamide;

- 2-[1-(dimethylamino)-1-methylethyl]-N-[4-fluoro-2-(methylsulfonyl)benzyl]-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(1-aminocyclopropyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(dimethylamino)cyclopropyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-[(pyrazin-2-ylcarbonyl)amino]cyclopropyl}pyrimidine-4-carboxamide;
 - benzyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)cyclopentylcarbamate;
- 15 2-(1-aminocyclopentyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-[1-(dimethylamino)cyclopentyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 20 2-(1-{[(ethylamino)carbonyl]amino}-1-methylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-[1-(benzylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
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 2-[1-(benzoylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-{1-[benzyl(methyl)amino]-1-methylethyl}-N-(4-fluorobenzyl)-5,6-30 dihydroxypyrimidine-4-carboxamide;
 - 2-[1-(dimethylamino)-1-methylethyl]-N-(2-ethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(2-chlorobenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;

N-(2-chlorobenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-5 carboxamide;

N-(5-chloro-2-methylbenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[(pyrazin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
 - 2-[1-(diethylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-morpholin-4-ylethyl)pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-piperidin-1-ylethyl)pyrimidine-4-20 carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-pyrrolidin-1-ylethyl)pyrimidine-4-carboxamide;
- 25 N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[methyl(pyridin-4-ylmethyl)amino]ethyl}pyrimidine-4-carboxamide;
 - 2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxy-N-[2-(methylthio)benzyl]pyrimidine-4-carboxamide;
- 30 N1,N1-diethyl-N~2~-[1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethyl]ethanediamide;
- 2-[1-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-1-methylethyl]-N-(4-fluorobenzyl)-5,6dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-{[(1-methyl-1H-imidazol-2-yl)carbonyl]amino}ethyl)pyrimidine-4-carboxamide;

5 N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-1-(4-oxopiperidin-1-yl)ethyl]pyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[methyl(pyridin-2-ylmethyl)amino]ethyl}pyrimidine-4-carboxamide;

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 $N-[1-(4-\{[(4-fluorobenzyl)amino]carbonyl\}-5,6-dihydroxypyrimidin-2-yl)-1-methylethyl]-4-methylmorpholine-2-carboxamide;$

2-{1-[acetyl(methyl)amino]-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

2-[1-(acetylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

20 2-{1-[4-(dimethylamino)piperidin-1-yl]-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(2,3-dimethoxybenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;

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2-[4-(dimethylamino)tetrahydro-2H-pyran-4-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(7-methyl-7-azabicyclo[2.2.1]hept-1-30 yl)pyrimidine-4-carboxamide;

2-(7-acetyl-7-azabicyclo[2.2.1]hept-1-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

2-(2-acetyl-2-azabicyclo[2.1.1]hex-1-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(2-methyl-2-azabicyclo[2.1.1]hex-1-5 yl)pyrimidine-4-carboxamide;
 - tert-butyl (2S,4R)-4-(benzyloxy)-2-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)piperidine-1-carboxylate;
- 2-[(2S,4R)-4-(benzyloxy)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6dihydroxypyrimidine-4-carboxamide;
 - 2-[(2S,4R)-4-(benzyloxy)-1-methylpiperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(2S,4R)-4-hydroxy-1-methylpiperidin-2-yl]pyrimidine-4-carboxamide;
 - 2-[1-acetyl-4-(benzyloxy)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-(1-ethyl-4-methylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[4-methyl-1-(pyrazin-2-ylcarbonyl)piperazin-2-yl]pyrimidine-4-carboxamide;
 - tert-butyl 3-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)thiomorpholine-4-carboxylate;
- 30 N-(4-fluorobenzyl)-5,6-dihydroxy-2-thiomorpholin-3-ylpyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylthiomorpholin-3-yl)pyrimidine-4-carboxamide;

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N-(4-fluorobenzyl)-5,6-dihydroxy-2-[4-(pyridin-2-ylcarbonyl)thiomorpholin-3-yl]pyrimidine-4-carboxamide;

2-(4-acetylthiomorpholin-3-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

tert-butyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-2-methoxyethylcarbamate;

- 2-[1-(dimethylamino)-2-methoxyethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-[1-(acetylamino)-2-methoxyethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(1-amino-2-methoxyethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-[(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-2-[1-(formylamino)-2-methoxyethyl]-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methoxy-1-(methylamino)ethyl]pyrimidine-4-carboxamide;
 - 2-{1-[acetyl(methyl)amino]-2-methoxyethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-[methyl(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(4R)-3-(pyridin-2-ylcarbonyl)-1,3-thiazolidin-4-yl]pyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(4R)-1,3-thiazolidin-4-yl]pyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(4R)-3-methyl-1,3-thiazolidin-4-yl]pyrimidine-4-carboxamide;
 - 2-(3-acetyl-1,3-thiazolidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 10 N-(4-fluorobenzyl)-5,6-dihydroxy-2-(3-methyl-1,3-thiazolidin-2-yl)pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1,2,4-trimethylpiperazin-2-yl)pyrimidine-4carboxamide;
 - $\hbox{$2-[2,4-dimethyl-1-(pyrazin-2-ylcarbonyl)piperazin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;}$
- 20 2-(1-acetyl-2,4-dimethylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - tert-butyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-2-methoxy-1-methylcarbamate;
- 25
 2-(1-amino-2-methoxy-1-methylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(acetylamino)-2-methoxy-1-methylethyl]-N-(4-fluorobenzyl)-5,6-30 dihydroxypyrimidine-4-carboxamide;
 - 2-[1-(dimethylamino)-2-methoxy-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methoxy-1-methyl-1-(methylamino)ethyl]pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-methyl-1-[(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
 - 2-(1,2-dimethylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-{1-[acetyl(methyl)amino]-2-methoxy-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-methyl-1-[methyl(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
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 2-{1-[(cyclohexylmethyl)(methyl)amino]-2-methoxy-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-{1-[(cyclohexylmethyl)amino]-2-methoxy-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-{1-[(cyclohexylmethyl)amino]-2-methoxy-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 25 2-(4-acetyl-1,2-dimethylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-(1-acetyl-2-methylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 30 N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methyl-1-(pyrazin-2-ylcarbonyl)piperidin-2-yl]pyrimidine-4-carboxamide;
- N-(2,3-dimethoxybenzyl)-2-(1,2-dimethylpiperidin-2-yl)-5,6-dihydroxypyrimidine-4carboxamide;

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N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methyl-1-(pyridin-2-ylcarbonyl)piperidin-2-yl]pyrimidine-4-carboxamide;

- 5 2-{1-[(2,4-dimethyl-1,3-thiazol-5-yl)carbonyl]-2-methylpiperidin-2-yl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
 - 2-[(2S)-1-acetyl-2-methylpyrrolidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

and pharmaceutically acceptable salts thereof.

Other embodiments of the present invention include the following:

- (a) A pharmaceutical composition comprising a compound of Formula (I) and a pharmaceutically acceptable carrier.
- (b) A pharmaceutical composition which comprises the product
 prepared by combining (e.g., mixing) an effective amount of a compound of Formula
 (I) and a pharmaceutically acceptable carrier.
 - (c) The pharmaceutical composition of (a) or (b), further comprising a therapeutically effective amount of an HIV infection/AIDS treatment agent selected from the group consisting of HIV/AIDS antiviral agents, immunomodulators, and anti-infective agents.
 - (d) The pharmaceutical composition of (c), wherein the HIV infection/AIDS treatment agent is an antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, and nucleoside HIV reverse transcriptase inhibitors.
 - (e) A combination useful for inhibiting HIV integrase, for treating or preventing infection by HIV, or for preventing, treating or delaying the onset of AIDS, which is a therapeutically effective amount of a compound of Formula (I) and a therapeutically effective amount of an HIV infection/AIDS treatment agent selected from the group consisting of HIV/AIDS antiviral agents, immunomodulators, and anti-infective agents.
 - (f) The combination of (e), wherein the HIV infection/AIDS treatment agent is an antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors and nucleoside HIV reverse transcriptase inhibitors.

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- (g) A method of inhibiting HIV integrase in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a compound of Formula (I).
- (h) A method of preventing or treating infection by HIV in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a compound of Formula (I).
- (i) The method of (h), wherein the compound of Formula (I) is administered in combination with a therapeutically effective amount of at least one antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, and nucleoside HIV reverse transcriptase inhibitors.
- (j) A method of preventing, treating or delaying the onset of AIDS in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a compound of Formula (I).
- (k) The method of (j), wherein the compound is administered in combination with a therapeutically effective amount of at least one antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, and nucleoside HIV reverse transcriptase inhibitors
- (l) A method of inhibiting HIV integrase in a subject in need thereof which comprises administering to the subject the pharmaceutical composition of (a), (b), (c) or (d) or the combination of (e) or (f).
- (m) A method of preventing or treating infection by HIV in a subject in need thereof which comprises administering to the subject the pharmaceutical composition of (a), (b), (c) or (d) or the combination of (e) or (f).
- (n) A method of preventing, treating or delaying the onset of AIDS in a subject in need thereof which comprises administering to the subject the pharmaceutical composition of (a), (b), (c) or (d) or the combination of (e) or (f).

The present invention also includes a compound of the present invention (i) for use in, (ii) for use as a medicament for, or (iii) for use in the preparation of a medicament for: (a) inhibiting HIV protease, (b) preventing or treating infection by HIV, or (c) preventing, treating or delaying the onset of AIDS. In these uses, the compounds of the present invention can optionally be employed in combination with one or more HIV/AIDS treatment agents selected from HIV/AIDS antiviral agents, anti-infective agents, and immunomodulators.

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Additional embodiments of the invention include the pharmaceutical compositions, combinations and methods set forth in (a)-(n) above and the uses set forth in the preceding paragraph, wherein the compound of the present invention employed therein is a compound of one of the embodiments, aspects, classes, subclasses, or features of the compounds described above. In all of these embodiments, the compound may optionally be used in the form of a pharmaceutically acceptable salt.

As used herein, the term "C₁₋₆ alkyl" (or "C₁-C₆ alkyl") means linear or branched chain alkyl groups having from 1 to 6 carbon atoms and includes all of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl. "C₁₋₄ alkyl" means n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl.

The term " C_0 " as employed in expressions such as " C_{0-6} alkyl" means a direct covalent bond. For example, when R^1 in Compound I is - C_{0-6} alkyl-O- C_{0-6} alkyl-Rk, then R^1 is -O-Rk when both alkyl groups are C_0 alkyl. Similarly, when an integer defining the presence of a certain number of atoms in a group is equal to zero, it means that the atoms adjacent thereto are connected directly by a bond. For

wherein p is an integer equal to zero, 1 or 2, then

ج R⁵

R⁴ has the following structure when p is zero:

The term "-C₁₋₆ alkyl-" refers to a C₁ to C₆ linear or branched alkyl group as just defined which is bivalent. It can alternatively be referred to as "C₁₋₆ alkylene" or "C₁₋₆ alkanediyl". A class of alkylenes of particular interest with respect to the invention is -(CH₂)₁₋₆-, and sub-classes of particular interest include -(CH₂)₁₋₄-, -(CH₂)₁₋₃-, -(CH₂)₁₋₂-, and -CH₂-.

The term "C₂₋₅ alkenyl" (or "C₂-C₅ alkenyl") means linear or branched chain alkenyl groups having from 2 to 5 carbon atoms and includes all of the pentenyl isomers as well as 1-butenyl, 2-butenyl, 3-butenyl, isobutenyl, 1-propenyl, 2-propenyl, and ethenyl (or vinyl). Similar terms such as "C₂₋₃ alkenyl" have an analogous meaning.

The term "-C₂₋₅ alkenyl-" refers to a C₂ to C₅ linear or branched alkenyl group as just defined which is bivalent. It can alternatively be referred to as "C₂₋₅ alkenylene" or "C₂₋₅ alkenediyl".

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The term "C₂₋₅ alkynyl" (or "C₂-C₅ alkynyl") means linear or branched chain alkynyl groups having from 2 to 5 carbon atoms and includes all of the pentynyl isomers as well as 1-butynyl, 2-butynyl, 3-butynyl, 1-propynyl, 2-propynyl, and ethynyl (or acetylenyl). Similar terms such as "C₂₋₃ alkynyl" have an analogous meaning.

The term "-C₂₋₅ alkynyl-" refers to a C₂ to C₅ linear or branched alkenyl group as just defined which is bivalent. It can alternatively be referred to as "C₂₋₅ alkynylene" or "C₂₋₅ alkynediyl".

The term "C3-8 cycloalkyl" (or "C3-C8 cycloalkyl") means a cyclic ring of an alkane having three to eight total carbon atoms (i.e., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, or cycloactyl). The terms "C3-7 cycloalkyl", "C3-6 cycloalkyl", "C5-7 cycloalkyl" and the like have analogous meanings.

The term "C₃₋₇ azacycloalkyl" (or "C₃-C₇ azacycloalkyl") means a saturated cyclic ring consisting of one nitrogen and from three to seven carbon atoms (i.e., azetidinyl, pyrrolidinyl, piperidinyl, or azepanyl).

The term "halogen" (or "halo") refers to fluorine, chlorine, bromine and iodine (alternatively referred to as fluoro, chloro, bromo, and iodo).

The term "C₁-6 haloalkyl" (which may alternatively be referred to as "C₁-C₆ haloalkyl" or "halogenated C₁-C₆ alkyl") means a C₁ to C₆ linear or branched alkyl group as defined above with one or more halogen substituents. The term "C₁-4 haloalkyl" has an analogous meaning. The term "C₁-6 fluoroalkyl" has an analogous meaning except that the halogen substituents are restricted to fluoro. Suitable fluoroalkyls include the series (CH₂)₀-4CF₃ (i.e., trifluoromethyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-n-propyl, etc.).

The term "carbocycle" (and variations thereof such as "carbocyclic" or "carbocyclyl") as used herein refers to (i) a C3 to C8 monocyclic, saturated or unsaturated ring, (ii) a C7 to C12 bicyclic ring system, or (iii) a C11 to C16 tricyclic ring system, wherein each ring in (ii) or (iii) is independent of or fused to the other ring or rings and each ring is saturated or unsaturated. The carbocycle may be attached to the rest of the molecule at any carbon atom which results in a stable compound. The fused bicyclic carbocycles are a subset of the carbocycles; i.e., the term "fused bicyclic carbocycle" generally refers to a C7 to C10 bicyclic ring system in which each ring is saturated or unsaturated and two adjacent carbon atoms are

shared by each of the rings in the ring system. Fused tricyclic carbocycles have an analogous meaning. A subset of the fused bicyclic carbocycles are those bicyclic carbocycles in which one ring is a benzene ring and the other ring is saturated or unsaturated, with attachment via any carbon atom that results in a stable compound. Representative examples of this subset include the following:

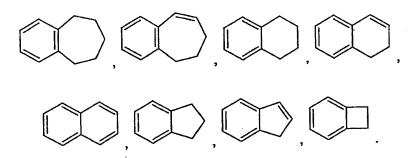
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The term "aryl" refers to aromatic mono- and poly-carbocyclic ring systems, wherein the individual carbocyclic rings in the polyring systems are fused or attached to each other via a single bond. Suitable aryl groups include phenyl, naphthyl, and biphenylenyl.

The term "heterocycle" (and variations thereof such as "heterocyclic" or "heterocyclyl") broadly refers to (i) a 4- to 8-membered, saturated or unsaturated monocyclic ring, (ii) a 7- to 12-membered bicyclic ring system, or (iii) an 11 to 16membered tricyclic ring system; wherein each ring in (ii) or (iii) is independent of or fused to, or bridged with, or spiro to the other ring or rings and each ring is saturated or unsaturated, and the monocyclic ring, bicyclic ring system, or tricyclic ring system contains one or more heteroatoms (e.g., from 1 to 6 heteroatoms, or from 1 to 4 heteroatoms) selected from N, O and S and a balance of carbon atoms (the monocylic ring typically contains at least one carbon atom and the ring systems typically contain at least two carbon atoms); and wherein any one or more of the nitrogen and sulfur heteroatoms is optionally be oxidized, and any one or more of the nitrogen heteroatoms is optionally quaternized. The heterocyclic ring may be attached at any heteroatom or carbon atom, provided that attachment results in the creation of a stable structure. When the heterocyclic ring has substituents, it is understood that the substituents may be attached to any atom in the ring, whether a heteroatom or a carbon atom, provided that a stable chemical structure results.

Saturated heterocyclics form a subset of the heterocycles; i.e., the term "saturated heterocyclic" generally refers to a heterocycle as defined above in which

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the entire ring system (whether mono- or poly-cyclic) is saturated. The term "saturated heterocyclic ring" refers to a 4- to 8-membered saturated monocyclic ring which consists of carbon atoms and one or more heteroatoms selected from N, O and S. Representative examples include piperidinyl, piperazinyl, azepanyl, pyrrolidinyl, pyrazolidinyl, imidazolidinyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, and tetrahydrofuryl (or tetrahydrofuranyl).

Heteroaromatics form another subset of the heterocycles; i.e., the term "heteroaromatic" (alternatively "heteroaryl") generally refers to a heterocycle as defined above in which the entire ring system (whether mono- or poly-cyclic) is an 10 aromatic ring system. The term "heteroaromatic ring" refers a 5- or 6-membered monocyclic aromatic ring which consists of carbon atoms and one or more heteroatoms selected from N, O and S. Representative examples of heteroaromatic rings include pyridyl, pyrrolyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl (or thiophenyl), thiazolyl, furanyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, and thiadiazolyl.

Representative examples of bicyclic heterocycles include benzotriazolyl, indolyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, isochromanyl, tetrahydroquinolinyl, quinolinyl, tetrahydroisoquinolinyl, isoquinolinyl, 2,3-dihydrobenzofuranyl, 7-

Representative examples of tricyclic heterocycles include phenothiazinyl, carbazolyl, beta-carbolinyl, tetrahydro-beta-carbolinyl, acridinyl, phenazinyl, and phenoxazinyl.

Unless expressly stated to the contrary, an "unsaturated" ring is a partially or fully unsaturated ring. For example, an "unsaturated monocyclic C6 carbocycle" refers to cyclohexene, cyclohexadiene, and benzene.

Unless expressly stated to the contrary, all ranges cited herein are inclusive. For example, a heterocycle described as containing from "1 to 4 heteroatoms" means the heterocycle can contain 1, 2, 3 or 4 heteroatoms.

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When any variable (e.g., Ra, Rb, Rc, Rk, etc.) occurs more than one time in any constituent or in Formula I or in any other formula depicting and describing compounds of the invention, its definition on each occurrence is independent of its definition at every other occurrence. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

The term "substituted" (e.g., as in "aryl which is optionally substituted with one or more substituents ...") includes mono- and poly-substitution by a named substituent to the extent such single and multiple substitution (including multiple substitution at the same site) is chemically allowed.

Substituted ring systems, which systems are themselves substituents bonded to a non-substituent atom, include, but are not limited to, moieties in which the atom bearing the ring substituent and the atom bonded to the non-substitutent atom are the same. For example, the substituent represented by



is a substituted cyclopropyl ring, wherein the cyclopropyl ring substituent is an amino group.

The compounds of the present invention may have asymmetric centers and may occur, except when specifically noted, as mixtures of stereoisomers or as individual diastereomers, or enantiomers, with all isomeric forms being included in the present invention.

The dihydroxypyrimidine compounds of the present invention (i.e., compounds of Formula I wherein $R^2 = H$) may also occur as tautomers thereof. Tautomers include, but are not limited to:

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$$R^1$$
 N R^4 R^1 N R^4 R^4

It is understood that the present invention includes all tautomers of the dihydroxy compounds embraced by Formula I, both singly and in mixtures.

The compounds of the present inventions are useful in the inhibition of

HIV integrase, the prevention or treatment of infection by human immunodeficiency
virus (HIV) and the prevention, treatment or the delay in the onset of consequent
pathological conditions such as AIDS. Preventing AIDS, treating AIDS, delaying the
onset of AIDS, or preventing or treating infection by HIV is defined as including, but
not limited to, treatment of a wide range of states of HIV infection: AIDS, ARC

(AIDS related complex), both symptomatic and asymptomatic, and actual or potential
exposure to HIV. For example, the compounds of this invention are useful in treating
infection by HIV after suspected past exposure to HIV by such means as blood
transfusion, exchange of body fluids, bites, accidental needle stick, or exposure to
patient blood during surgery.

The compounds of this invention are useful in the preparation and execution of screening assays for antiviral compounds. For example, the compounds of this invention are useful for isolating enzyme mutants, which are excellent screening tools for more powerful antiviral compounds. Furthermore, the compounds of this invention are useful in establishing or determining the binding site of other antivirals to HIV integrase, e.g., by competitive inhibition. Thus the compounds of this invention are commercial products to be sold for these purposes.

Compounds representative of the present invention have been tested for inhibition in an assay for the strand transfer activity of integrase. The assay is conducted in accordance with Wolfe, A.L. et al., J. Virol. 1996, 70: 1424-1432, for recombinant integrase, except that: (i) the assay uses preassembled integrase strand transfer complexes; (ii) the strand transfer reaction is performed in the presence of inhibitor in 2.5 mM MgCl₂ using 0.5 to 5 nM of a 3' FITC labeled target DNA substrate as described in WO 02/30930, the disclosure of which is hereby incorporated by reference, and (iii) strand transfer products are detected using an alkaline phosphatase conjugated anti-FITC antibody and a chemiluminescent alkaline

phosphatase substrate. Representative compounds (e.g., the compounds set forth in Tables 1-25 below) tested in the integrase assay demonstrated IC50's of about 5 micromolar or less.

Further description on conducting the assay using preassembled complexes is found in Hazuda et al., *J. Virol.* 1997, <u>71</u>: 7005-7011; Hazuda et al., *Drug Design and Discovery* 1997, <u>15</u>: 17-24; and Hazuda et al., *Science* 2000, <u>287</u>: 646-650.

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Certain compounds representative of the present invention have also been tested in an assay for inhibition of acute HIV infection of T-lymphoid cells, conducted in accordance with Vacca, J.P. et al., *Proc. Natl. Acad. Sci. USA* 1994, <u>91</u>: 4096. These compounds demonstrated IC95's of about 10 micromolar or less.

The compounds of the present invention may be administered in the form of pharmaceutically acceptable salts. The term "pharmaceutically acceptable salt" refers to a salt which possesses the effectiveness of the parent compound and which is not biologically or otherwise undesirable (e.g., is neither toxic nor otherwise deleterious to the recipient thereof). Suitable salts include acid addition salts which may, for example, be formed by mixing a solution of the compound of the present invention with a solution of a pharmaceutically acceptable acid such as hydrochloric acid, sulfuric acid, acetic acid, trifluoroacetic acid, or benzoic acid. When the compounds of the invention carry an acidic moiety, suitable pharmaceutically acceptable salts thereof can include alkali metal salts (e.g., sodium or potassium salts), alkaline earth metal salts (e.g., calcium or magnesium salts), and salts formed with suitable organic ligands such as quaternary ammonium salts. Also, in the case of an acid (-COOH) or alcohol group being present, pharmaceutically acceptable esters can be employed to modify the solubility or hydrolysis characteristics of the compound.

For the purpose of preventing or treating HIV infection or preventing, treating or delaying the onset of AIDS, the compounds of the present invention may be administered orally, parenterally (including subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques), by inhalation spray, or rectally, in the form of a unit dosage of a pharmaceutical composition containing a therapeutically effective amount of the compound and conventional non-toxic pharmaceutically-acceptable carriers, adjuvants and vehicles.

The term "administration" and variants thereof (e.g., "administering" a compound) in reference to a compound of the invention mean providing the compound or a prodrug of the compound to the individual in need of treatment.

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When a compound of the invention or a prodrug thereof is provided in combination with one or more other active agents (e.g., antiviral agents useful for treating HIV infection or AIDS), "administration" and its variants are each understood to include concurrent and sequential provision of the compound or prodrug and other agents.

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combining the specified ingredients in the specified amounts.

By "pharmaceutically acceptable" is meant that the ingredients of the pharmaceutical composition must be compatible with each other and not deleterious to the recipient thereof.

The term "subject" (alternatively referred to herein as "patient") as used herein refers to an animal, preferably a mammal, most preferably a human, who has been the object of treatment, observation or experiment.

The term "therapeutically effective amount" as used herein means that amount of active compound or pharmaceutical agent that elicits the biological or medicinal response in a tissue, system, animal or human that is being sought by a researcher, veterinarian, medical doctor or other clinician, which includes alleviation of the symptoms of the disease being treated. When the active compound (i.e., active ingredient) is administered as the salt, references to the amount of active ingredient are to the free acid or free base form of the compound.

The pharmaceutical compositions may be in the form of orally-administrable suspensions or tablets or capsules, nasal sprays, sterile injectible preparations, for example, as sterile injectible aqueous or oleagenous suspensions or suppositories. These compositions can be prepared by methods and contain excipients which are well known in the art. Suitable methods and ingredients are described in Remington's Pharmaceutical Sciences, 18th edition, edited by A. R. Gennaro, Mack Publishing Co., 1990, which is herein incorporated by reference in its entirety.

The compounds of this invention can be administered orally in a dosage range of 0.001 to 1000 mg/kg of mammal (e.g., human) body weight in divided doses. One preferred dosage range is 0.01 to 500 mg/kg body weight orally in divided doses. Another preferred dosage range is 0.1 to 100 mg/kg body weight orally in divided doses. For oral administration, the compositions can be provided in the form of tablets or capsules containing 1.0 to 500 milligrams of the active ingredient,

particularly 1, 5, 10, 15, 20, 25, 50, 75, 100, 150, 200, 250, 300, 400, and 500 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. The specific dose level and frequency of dosage for any particular patient may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular condition, and the host undergoing therapy.

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As noted above, the present invention is also directed to use of the HIV integrase inhibitor compounds of the present invention with one or more agents useful in the treatment of HIV infection or AIDS. For example, the compounds of this invention may be effectively administered, whether at periods of pre-exposure and/or post-exposure, in combination with effective amounts of one or more of the HIV/AIDS antivirals, imunomodulators, antiinfectives, or vaccines useful for treating HIV infection or AIDS. Suitable antiviral agents include those listed in the following Table:

ANTIVIRALS

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Drug Name	Manufacturer (Tradename and/or Location)	Indication (Activity)
abacavir GW 1592 1592U89	Glaxo Welcome (ZIAGEN®)	HIV infection, AIDS, ARC (nRTI)
abacavir + lamivudine + zidovudine	GlaxoSmithKline (TRIZIVIR®)	HIV infection, AIDS, ARC (nnRTI)
acemannan	Carrington Labs (Irving, TX)	ARC
ACH 126443	Achillion Pharm.	HIV infections, AIDS, ARC (nucleoside reverse transcriptase inhibitor)
acyclovir	Burroughs Wellcome	HIV infection, AIDS, ARC, in combination with AZT
AD-439	Tanox Biosystems	HIV infection, AIDS, ARC
AD-519	Tanox Biosystems	HIV infection, AIDS, ARC
adefovir dipivoxil GS 840	Gilead	HIV infection, AIDS, ARC (RTI)
AL-721	Ethigen (Los Angeles, CA)	ARC, PGL, HIV positive, AIDS
alpha interferon	Glaxo Wellcome	Kaposi's sarcoma, HIV, in combination w/Retrovir
AMD3100	AnorMed	HIV infection, AIDS, ARC (CXCR4 antagonist)
amprenavir 141 W94 GW 141 VX478 (Vertex)	Glaxo Wellcome (AGENERASE®)	HIV infection, AIDS, ARC (PI)
ansamycin LM 427	Adria Laboratories (Dublin, OH) Erbamont (Stamford, CT)	ARC
antibody which neutralizes pH labile alpha aberrant Interferon	Advanced Biotherapy Concepts (Rockville, MD)	AIDS, ARC

AR177	Aronex Pharm	HIV infection, AIDS, ARC
atazanavir (BMS 232632)	Bristol-Myers-Squibb (ZRIVADA®)	HIV infection, AIDS, ARC (PI)
beta-fluoro-ddA	Nat'l Cancer Institute	AIDS-associated diseases
BMS-232623 (CGP-73547)	Bristol-Myers Squibb/ Novartis	HIV infection, AIDS, ARC (PI)
BMS-234475 (CGP-61755)	Bristol-Myers Squibb/ Novartis	HIV infection, AIDS, ARC (PI)
capravirine (AG-1549, S-1153)	Pfizer	HIV infection, AIDS, ARC (nnRTI)
CI-1012	Warner-Lambert	HIV-1 infection
cidofovir	Gilead Science	CMV retinitis, herpes, papillomavirus
curdlan sulfate	AJI Pharma USA	HIV infection
cytomegalovirus immune	MedImmune	CMV retinitis
cytovene ganciclovir	Syntex	sight threatening CMV peripheral CMV retinitis
delavirdine	Pharmacia-Upjohn (RESCRIPTOR®)	HIV infection, AIDS, ARC (nnRTI)
dextran Sulfate	Ueno Fine Chem. Ind. Ltd. (Osaka, Japan)	AIDS, ARC, HIV positive asymptomatic
ddC (zalcitabine, dideoxycytidine)	Hoffman-La Roche (HIVID®)	HIV infection, AIDS, ARC (nRTI)
ddI Dideoxyinosine	Bristol-Myers Squibb (VIDEX®)	HIV infection, AIDS, ARC; combination with AZT/d4T (nRTI)
DPC 681 & DPC 684	DuPont	HIV infection, AIDS, ARC (PI)
DPC 961 & DPC 083	DuPont	HIV infection AIDS, ARC (nnRTRI)
emvirine	Triangle Pharmaceuticals (COACTINON®)	HIV infection, AIDS, ARC (non-nucleoside reverse transcriptase inhibitor)

EL10	Elan Corp, PLC (Gainesville, GA)	HIV infection
efavirenz (DMP 266)	DuPont (SUSTIVA®) Merck (STOCRIN®)	HIV infection, AIDS, ARC (nnRTI)
famciclovir	Smith Kline	herpes zoster, herpes simplex
emtricitabine FTC	Triangle Pharmaceuticals (COVIRACIL®) Emory University	HIV infection, AIDS, ARC (nRTI)
emvirine	Triangle Pharmaceuticals (COACTINON®)	HIV infection, AIDS, ARC (non-nucleoside reverse transcriptase inhibitor)
нв ү 097	Hoechst Marion Roussel	HIV infection, AIDS, ARC (nnRTI)
hypericin	VIMRx Pharm.	HIV infection, AIDS, ARC
recombinant human interferon beta	Triton Biosciences (Almeda, CA)	AIDS, Kaposi's sarcoma, ARC
interferon alfa-n3	Interferon Sciences	ARC, AIDS
indinavir	Merck (CRIXIVAN®)	HIV infection, AIDS, ARC, asymptomatic HIV positive, also in combination with AZT/ddI/ddC (PI)
ISIS 2922	ISIS Pharmaceuticals	CMV retinitis
JE2147/AG1776	Agouron	HIV infection, AIDS, ARC (PI)
KNI-272	Nat'l Cancer Institute	HIV-assoc. diseases
lamivudine, 3TC	Glaxo Wellcome (EPIVIR®)	HIV infection, AIDS, ARC; also with AZT (nRTI)
lobucavir	Bristol-Myers Squibb	CMV infection
lopinavir (ABT-378)	Abbott	HIV infection, AIDS, ARC (PI)
lopinavir + ritonavir (ABT-378/r)	Abbott (KALETRA®)	HIV infection, AIDS, ARC (PI)

mozenavir (DMP-450)	AVID (Camden, NJ)	HIV infection, AIDS, ARC (PI)
nelfinavir	Agouron (VIRACEPT®)	HIV infection, AIDS, ARC (PI)
nevirapine	Boeheringer Ingleheim (VIRAMUNE®)	HIV infection, AIDS, ARC (nnRTI)
novapren	Novaferon Labs, Inc. (Akron, OH)	HIV inhibitor
pentafusaide T-20	Trimeris	HIV infection, AIDS, ARC (fusion inhibitor)
peptide T octapeptide sequence	Peninsula Labs (Belmont, CA)	AIDS
PRO 542	Progenics	HIV infection, AIDS, ARC (attachment inhibitor)
PRO 140	Progenics	HIV infection, AIDS, ARC (CCR5 co-receptor inhibitor)
trisodium phosphonoformate	Astra Pharm. Products, Inc	CMV retinitis, HIV infection, other CMV infections
PNU-140690	Pharmacia Upjohn	HIV infection, AIDS, ARC (PI)
probucol	Vyrex	HIV infection, AIDS
RBC-CD4	Sheffield Med. Tech (Houston TX)	HIV infection, AIDS, ARC
ritonavir (ABT-538)	Abbott (RITONAVIR®)	HIV infection, AIDS, ARC (PI)
saquinavir	Hoffmann-LaRoche (FORTOVASE®)	HIV infection, AIDS, ARC (PI)
stavudine; d4T didehydrodeoxy- thymidine	Bristol-Myers Squibb (ZERIT®)	HIV infection, AIDS, ARC (nRTI)
T-1249	Trimeris	HIV infection, AIDS, ARC (fusion inhibitor)
TAK-779	Takeda	HIV infection, AIDS, ARC (injectable CCR5 receptor antagonist)

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tenofovir	Gilead (VIREAD®)	HIV infection, AIDS, ARC (nRTI)
tipranavir (PNU-140690)	Boehringer Ingelheim	HIV infection, AIDS, ARC (PI)
TMC-120 & TMC-125	Tibotec	HIV infections, AIDS, ARC (nnRTI)
TMC-126	Tibotec	HIV infection, AIDS, ARC (PI)
valaciclovir	Glaxo Wellcome	genital HSV & CMV infections
virazole ribavirin	Viratek/ICN (Costa Mesa, CA)	asymptomatic HIV positive, LAS, ARC
zidovudine; AZT	Glaxo Wellcome (RETROVIR®)	HIV infection, AIDS, ARC, Kaposi's sarcoma in combination with other therapies (nRTI)

PI = protease inhibitor nnRTI = non-nucleoside reverse transcriptase inhibitor nRTI = nucleoside reverse transcriptase inhibitor

A compound of the present invention can also be administered in combination with another HIV integrase inhibitor such as a compound described in WO 99/62513,WO 99/62520, or WO 99/62897. A compound of the present invention can also be administered in combination with a CCR5 receptor antagonist, such as a compound described in WO 99/04794, WO 99/09984, WO 99/38514, WO 00/59497, WO 00/59498, WO 00/59502, WO 00/59503, WO 00/76511, WO 00/76512, WO 00/76513, WO 00/76514, WO 00/76792, or WO 00/76793. The compounds of this invention may be effectively administered, whether at periods of pre-exposure and/or post-exposure, in combination with effective amounts of one or more HIV/AIDS antivirals, immunomodulators, antiinfectives, or vaccines useful for treating HIV infection or AIDS disclosed in the Table in WO 01/38332, which is herein incorporated by reference in its entirety.

It will be understood that the scope of combinations of the compounds of this invention with HIV/AIDS antivirals, immunomodulators, anti-infectives or vaccines is not limited to the list in the above-referenced Table in WO 01/38332, but includes in principle any combination with any pharmaceutical composition useful for

the treatment of AIDS. The HIV/AIDS antivirals and other agents will typically be employed in these combinations in their conventional dosage ranges and regimens as reported in the art, including the dosages described in the <u>Physicians' Desk Reference</u>, 54th edition, Medical Economics Company, 2000. The dosage ranges for a compound of the invention in these combinations are the same as those set forth above.

Abbreviations used in the instant specification, particularly the Schemes and Examples, include the following:

AIDS = acquired immunodeficiency syndrome

ARC = AIDS related complex

BOC or Boc = t-butyloxycarbonyl

Bn = benzylBz = benzoyl

CBZ or Cbz = carbobenzoxy (alternatively, benzyloxycarbonyl)

DMAD = dimethylacetylenedicarboxylate

DMF = N,N-dimethylformamide

Et = ethyl

FIA-MS = flow injection analysis mass spectrometry

HIV = human immunodeficiency virus

HPLC = high performance liquid chromatography

20 Me = methyl

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NMP = N-methyl pyrrolidinone

NMR = nuclear magnetic resonance

Ph = phenyl

TFA = trifluoroacetic acid

25 THF = tetrahydrofuran

The compounds of the present invention can be readily prepared according to the following reaction schemes and examples, or modifications thereof, using readily available starting materials and reagents. In these reactions, it is also possible to make use of variants which are themselves known to those of ordinary skill in this art, but are not mentioned in greater detail. Furthermore, other methods for preparing compounds of the invention will be readily apparent to the person of ordinary skill in the art in light of the following reaction schemes and examples. Unless otherwise indicated, all variables are as defined above.

The compounds of the present invention can be prepared by coupling suitable alkyl 2-substituted-5,6 dihydroxypyrimidine-4-carboxylates (or the

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corresponding carboxylic acids or acid derivatives such as acid halides) with the appropriate amines, as represented by General Scheme below. In the scheme, P1 and P2 are H or protective groups, typically esters (e.g., benzoate or pivalate) that are normally removed under the conditions employed to convert the -COOR^ ester to the amide. The ester protective groups are typically used to purify the 2-substituted-5,6 dihydroxypyrimidine-4-carboxylates after their synthesis when the unprotected product cannot be crystallized from the reaction crude and/or for synthetic reasons.

General Scheme

Compound I

$$P^1=P^2=H$$
 $P^1=P^2=H$
 $P^1=$

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Methods for coupling carboxylic acid derivatives with amines to form carboxamides are well known in the art. Suitable methods are described, for example, in Jerry March, Advanced Organic Chemistry, 3rd edition, John Wiley & Sons, 1985, pp. 370-376. Amines of formula 1-1 can be prepared using the methods described in Richard Larock, Comprehensive Organic Transformations, VCH Publishers Inc, 1989, pp 385-438, or routine variations thereof. Methyl-2-sustituted-5,6-dihydroxypyrimidine-4-carboxylate of formula 1-2 can be prepared using methods described in Culbertson et al., J Heterocycl. Chem. 1979, 16 (7): 1423-24. The

procedures and schemes below illustrate and expand upon the chemistry portrayed in the General Scheme.

Scheme A depicts the synthesis of 2-substituted-5,6-dihydroxypyrimidine-4-carboxamide (2-3). The methyl-5,6-dihydroxypyrimidine-4-carboxylate 2-2 can be obtained by reacting the appropriate amidoxime 2-1 with dimethylacetylenedicarboxylate, followed by cyclization at high temperature in appropriate solvent. The methyl ester 2-2 can be reacted with the amine in solvents like DMF, methanol, ethanol, toluene, NMP, at the appropriate temperature to give the final compound 2-3. Amidoximes 2-1 can be prepared from the corresponding nitriles by chemistry described herein (see Example 5, Step 4 or Example 6, Step 1). Nitriles can be prepared from carboxylic acids by various procedures, including, for example, conversion to carboxamides by the procedure of Pozdnev, *Tetrahedron Lett.* 1989, 30: 5193), and dehydration by the procedure of Waldmann, *Tetrahedron* 1994, 50: 11865) (see Example 5, Step 3). Compound 2-2 can be recovered by precipitation and filtration from the cooled reaction mixture. Scheme A is exemplified in Example 1 below.

SCHEME A:

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Part 1 of Scheme B depicts a general synthesis of compounds bearing a nucleophilic group (e.g., an amine) in the 2-substituent. After bromination of a

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-CH₂Br (or -CH₂Cl) group using standard chemistry, the bromo (or chloro) derivative 3-1 can be treated with a nucleophile ("Nu"; e.g., an amine, thiol, or alcoholate) and, without isolation of the nucleophile-substituted ester intermediate 3-2, then with the amine 1-1 to give the final product 3-3. Part 1 of Scheme B is exemplified in

Example 2 below. Part 2 of Scheme B shows a variation of Part 1, wherein the site of nucleophilic substitution is -CHBr- (or -CHCl-). Scheme B, Part 2 is exemplified in Example 3 below.

Scheme B

10 Part 1

3-6

Part 2

Scheme C shows a method for preparing compounds of the present invention that contain an alkylated aliphatic amine in the substituent at the 2 position. Nitrogen alkylation is achieved via a reductive amination. There are two equivalent 5 synthetic strategies within the scope of Scheme C: reductive alkylation on the pyrimidine methyl ester followed by synthesis of the carboxamide or, alternatively, synthesis of the carboxamide followed by reductive amination. A deprotection step can be employed as neeeded. Example 4 below illustrates the application of Scheme C for preparing a compound with an acyclic aliphatic amine in the 2-position, wherein 10 the CBZ-protected pyrimidine derivative was converted to the corresponding benzylic amide. Example 5 below describes the preparation of a compound with a cyclic amne in the 2 position in which Scheme C was used in the final two steps. Example 6 below illustrates the application of Scheme C to the preparation of a compound with a pyrrolidine in the 2-position. Example 7 describes the alkylation of a compound with 15 a piperazine in the 2-position.

Scheme C

Scheme D presents an alternative approach to the preparation of compounds bearing a cyclic aliphatic tertiary amine as 2-substituents of the pyrimidine core, wherein the alkylation of the secondary amine with an alkyl halide is followed by synthesis of the benzylic amide with concomitant deprotection of the benzoate ester. Scheme D is exemplified in Example 8 below.

Scheme D

Scheme E shows the preparation of compounds of the present invention of formula 6-2 by reaction of aldehydes or ketones 6-1 with suitable amines under reductive alkylation conditions. Scheme E is exemplified in Example 9 below.

Scheme E

C = absent, alkyl, or aryl

P¹, P² = H or protective group

R^w = H, alkyl, or aryl

R^x = H, alkyl, or aryl

or R^x and R^y together with the N

to which they are attached

form an N-containing heterocycle

Scheme F shows a procedure for preparing compounds of the present invention which are unsubstituted in the 2 position. The pyrimidine monocarboxylic acid 7-1 can be decarboxylated in acid solution to the 2-unsubstituted pyrimidine 7-2, which can be further elaborated to the amide 7-3. Scheme F is exemplified in Example 10 below.

Scheme F

$$OP^{2}$$
 OP^{1}
 O

Synthesis of compounds of general formula 8-3 can be achieved as

depicted in Scheme G. The synthetic strategy is based on the reaction of a pyrimidine bearing an aminoaromatic system in the 2 position (8-1) with an isocyanate in the presence of a base and the resulting urea 8-2 can then be converted into the final amide 8-3. Scheme G is exemplified in Example 11 below.

Scheme G

The preparation of compounds that feature a carboxamide at the 2 position of the pyrimidine core can be achieved as shown in Scheme H. Reaction of 4-ethyl-2-methyl-5,6-dihydroxypyrimidine-2,4-dicarboxylate (9-1) with a suitable amine affords regioselectively the 4-carboxamide (9-2), which can subsequently be converted into the 2,4-dicarboxamide derivative (9-3) by further reaction with an amine. Scheme H is exemplified in Example 12 below.

Scheme H

EtO
$$\stackrel{OP^2}{N} \stackrel{OP^1}{OCH_3} \stackrel{R^3}{\longrightarrow} \stackrel{OH}{N} \stackrel{OH}{N} \stackrel{OH}{N} \stackrel{R^3}{\nearrow} \stackrel{P^3}{\longrightarrow} \stackrel{N}{N} \stackrel{N}{\nearrow} \stackrel{R^3}{\longrightarrow} \stackrel{N}{N} \stackrel{N}{\nearrow} \stackrel{N} \stackrel{N}{\nearrow} \stackrel{N}{\nearrow} \stackrel{N}{\nearrow} \stackrel{N}{\nearrow} \stackrel{N}{\nearrow} \stackrel{N}{\nearrow} \stackrel{N}{\nearrow} \stackrel{N}{\nearrow$$

Compounds of the present invention with general formula 10-3

5 containing an acylated nitrogen or sulfonylated nitrogen in the substituent at the 2position, can be prepared following Scheme I. Acylation or sulfonylation of the
nitrogen in the 2-substituent of the pyrimidine core provides compound 10-2, which
can be elaborated into the final amide 10-3. Scheme I is exemplified in Examples 13
and 14 below.

Scheme I

Compounds of the present invention bearing an alkoxy substituent on the 6 position of the pyrimidine core can be synthesized as shown in Scheme J. The synthetic pathway is based on the reaction of pyrimidine 11-1, suitably protected on the 5-hydroxyl group, with an alkylating agent (such as an halide or a sulphate). Intermediate 11-2 can be further elaborated into the amide 11-3 following the usual chemistry. Scheme J is exemplified in Example 15 below.

Scheme J

Compounds of the present invention with general formula 14-1 containing a tertiary amine at the 2-position of the pyrimimidine core can be prepared according to general procedure describe in scheme K. The N,N dimethyl amine present at the two position of C-4 can be replace with another amine by mixing and heating the substrate and regent in appropriate solvent to afford the desired product 14-1. Scheme K is exemplified in Example 16 reported below.

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Scheme K:

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In the processes for preparing compounds of the present invention set forth in the foregoing schemes and exemplified in the examples below, functional groups in various moieties and substituents may be sensitive or reactive under the reaction conditions employed and/or in the presence of the reagents employed. Such sensitivity/reactivity can interfere with the progress of the desired reaction to reduce the yield of the desired product, or possibly even preclude its formation. Accordingly, it may be necessary or desirable to protect sensitive or reactive groups on any of the molecules concerned. Protection can be achieved by means of conventional protecting groups, such as those described in Protective Groups in Organic Chemistry, ed. J.F.W. McOmie, Plenum Press, 1973 and in T.W. Greene & P.G.M. Wuts, Protective Groups in Organic Synthesis, John Wiley & Sons, 1991. The protecting groups can be removed at a convenient subsequent stage using methods known in the art. For example, in preparing the compounds of the invention it is sometimes necessary to protect one or more amino groups (e.g., amino groups present in substituents at the 2-position of the pyrimidine ring) with, for example, a Boc or Cbz group; or to protect hydroxy (e.g., the 5,6-dihydroxy groups on the pyrimidine ring) with, for example, a benzoyl, benzyl, or pivaloyl group. The Boc group can be removed by acid treatment (e.g., TFA) either before or after formation of the final amide at C-4 of the pyrimidine nucleus. The Cbz and benzyl groups are typically removed by catalytic hydrogenation or under strong acid conditions, either prior to or following formation of the final amide. The benzoyl or pivaloyl group can be removed concurrently with the formation of the final amide. Examples 4 and 6 below illustrate the use of a Cbz protective group and of Boc and benzoyl protective groups in the preparation of compounds of the invention.

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The following examples serve only to illustrate the invention and its practice. The examples are not to be construed as limitations on the scope or spirit of the invention.

EXAMPLE 1

N-(4-fluorobenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide

Methyl 5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxylate (A-2). Step 1:

N'-hydroxythiophene-2-carboximidamide (A-1) (amidoxine synthesis 5 is exemplified below - see compounds C-8 and C-14)was suspended in chloroform and refluxed overnight in the presence of 1.0 eq. of dimethylacetylenedicarboxylate. After cooling to room temperature, volatiles were evaporated and the residue was refluxed in xylene for 3 hr. The mixture was cooled to room temperature to allow the formation of a precipitate. The title product (A-2) was collected by filtration and 10 washed with diethyl ether several times.

 1 H NMR (DMSO-d₆, 300 MHz) δ 13.0 (bs, 1 H), 8.08 (d, J =3.2 Hz, 1 H), 7.85 (d, J=4.4 Hz, 1 H), 7.25 (dd, J=4.9 Hz, J=3.9 Hz, 1 H), 3.93 (s, 3 H).

N-(4-fluorobenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-Step 2: 15 carboxamide (A-3).

Methyl 5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxylate (A-2) was dissolved in DMF and 2.0 eq. of 4-fluorobenzylamine were added to the stirred solution. Reaction mixture was left overnight at 90 °C. After cooling to room temperature 1 N HCl was added and a solid precipitated from the mixture. This solid was collected by filtration, washed with ethyl ether and dried under vacuum to afford the compound (A-3).

 1 H NMR (DMSO-d₆, 300 MHz) δ 13.0 (s, 1 H), 12.5 (s, 1H), 9.18 (bs, 1 H), 8.03 (d, J=3.0 Hz, 1 H), 7.81 (d, J = 4.8 Hz, 1 H), 7.39 (dd, J = 5.7 Hz, J = 8.4 Hz, 2 H), 7.19-

7.2 (m, 3 H), 4.51 (d, J = 6.3 Hz, 2 H). 25

MS m/z 346 (M+H)*.

EXAMPLE 2

2-{4-[(Diethylamino)methyl]phenyl}-N-(2,3-dimethoxybenzyl)-5,6dihydroxypyrimidine-4-carboxamide

$$H_3C$$
 H_3C
 OH
 OH
 OH
 H
 OCH_3

Methyl 5,6-bis(benzoyloxy)-2-(4-methylphenyl)pyrimidine-4-Step 1: carboxylate (B-2).

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A mixture of dihydroxypyrimidine methylcarboxylate (B-1) (prepared from 4-methylbenzonitrile by procedures similar to those set forth in Scheme A), 4 eq. of benzoylchloride and 8 eq. of dry pyridine was stirred in dry dichloromethane at room temperature over night. The reaction mixture was diluted with EtOAc and the organic layer was washed twice with 1N HCl, once with brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The solid residue was triturated with diethyl ether to give product (B-2). ¹H-NMR (CDCl₃, 400 MHz) δ 8.38 (d, J = 8.2 Hz, 2 H), 8.14 (d, J = 7.44 Hz, 2 H), 8.10 (d, J = 7.44 Hz, 2 H), 7.62 (m, 2 H), 7.45 (m, 4 H), 7.3 (d, J = 8.06 Hz, 2 H),

3.93 (s, 3 H), 2.44 (s, 3 H). 20

> Methyl 5,6-bis(benzoyloxy)-2-[4-(bromomethyl)phenyl]pyrimidine-4-Step 2: carboxylate (B-3).

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A suspension of methyl ester (B-2), an equimolar amount of N-bromosuccinimide and 5 % of dibenzoylhydroperoxide in carbon tetrachloride was heated at 95°C. The reaction mixture was refluxed for 2 hrs, then allowed to cool at room temperature. Succinimide was filtered off and volatiles were removed *in vacuo* to give the desired product (B-3) as a white solid after treatment with petroleum ether. 1 H-NMR (CDCl₃, 400 MHz) δ 8.47 (d, J=8.25 Hz, 2 H), 8.14 (d, J=7.56 Hz, 2 H), 8.10 (d, J=7.50 Hz, 2 H), 7.63 (m, 2 H), 7.53 (d, J=8.23 Hz, 2 H), 7.46 (m, 4 H), 4.56 (s, 2 H), 3.94 (s, 3 H).

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Step 3: 2-{4-[(Diethylamino)methyl]phenyl}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (**B-4**).

A mixture of the benzylic bromide (B-3) and diethylamine (4 eq.) in THF was allowed to stir at room temperature overnight. The volatiles were then removed *in vacuo*, the residue was taken up in DMF and after the addition of a slight excess of 2,3-dimethoxybenzylamine the reaction mixture was stirred at 90°C over night. 1N HCl was then added to the reaction mixture and the crude product was purified by preparative HPLC (C18, CH₃CN/H₂O, 0.1% trifluoroacetic acid) to obtain title compound (B-4) as the trifluoroacetate salt.

¹H-NMR (DMSO-d₆, 400 MHz) δ 13.01 (bs, 1 H), 12.57 (s, 1 H), 9.53 (bs, 1 H), 9.36 (bs, 1 H), 8.34 (d, *J*=8.32 Hz, 2 H), 7.63 (d, *J*=8.27 Hz, 2 H), 7.08-6.96 (m, 2 H), 6.80 (m, 1 H), 4.52 (d, *J*=6.36 Hz, 2 H), 4.37 (d, *J*=4.35 Hz, 2 H), 3.82 (s,3 H), 3.08 (m, 4 H), 1.22 (t, *J*=7.20 Hz, 6 H). MS *m/z* 467 (M+H)[†].

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EXAMPLE 3

2-[(Dimethylamino)(phenyl)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide

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Step 1: Methyl-5,6-bis(benzoyloxy)-2-benzylpyrimidine-4-carboxylate (B-6).

To a stirred solution of methyl-2-benzyl-5,6-dihydroxypyrimidine-4-carboxylate (B-5) (1.0 eq.) (prepared from phenylacetonitrile by procedures similar to those set forth in Scheme A) in anhydrous pyridine, benzoyl chloride (5.0 eq.) was added dropwise with external cooling and the reaction was stirred overnight at room temperature. The mixture was poured into 1N HCl and extracted with EtOAc. The organic phase was washed with a saturated solution of NaHCO₃ and with brine, dried (Na₂SO₄), filtered and concentrated under vacuum. The residue was purified by flash column chromatography (SiO₂, 80/20 v/v petroleum ether/ ethyl acetate as eluent) to give the title compound (B-6) as a colorless oil.

¹H NMR (CDCl₃) δ 8.07 (t, J=9.0 Hz, 4 H), 7.62-7.57 (m, 2 H), 7.48-7.40 (m, 6 H), 7.31 (t, J=8.9 Hz, 2 H), 7.28 (d, J=8.9 Hz, 1 H), 4.41 (s, 2 H), 3.91 (s, 3 H).

Step 2: Methyl-5,6-bis(benzoyloxy)-2-[bromo(phenyl)methyl]pyrimidine-4-carboxylate (B-7).

A solution of methyl-5,6-bis(benzoyloxy)-2-benzylpyrimidine-4-carboxylate (B-6) (1.0 eq.) in carbon tetrachloride was heated up to 90 °C under nitrogen; N-bromosuccinimide (1.0 eq.) and benzoyl peroxide (0.1 eq.) were added as dry powder and mixture was refluxed for 3 h. After cooling, succinimide was removed by filtration and the filtrate was concentrated and purified by flash column chromatography (SiO₂, 85/15 v/v petroleum ether/ ethyl acetate as eluent) to give the title product (B-7).

¹H NMR (CDCl₃) δ 8.11 (d, J=8.6 Hz, 2 H), 8.05 (d, J=8.6 Hz, 2 H), 7.79 (d, J=8.9 Hz, 2 H), 7.56-7.49 (m, 2 H), 7.50-7.30 (m, 7 H), 6.30 (s, 1 H), 3.90 (s, 3 H).

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Step 3: 2-[(Dimethylamino)(phenyl)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (**B-8**).

Methyl-5,6-bis(benzoyloxy)-2-[bromo(phenyl)methyl]pyrimidine-4-carboxylate (B-7) was added to 2.0M solution of dimethylamine in THF. After stirring the mixture for 10 min at room temperature, volatiles were evaporated by bubbling N₂ through the solution and 4 eq. of 4-fluorobenzylamine in DMF were added. Reaction mixture was stirred at 90 °C for 1 h. After cooling to room temperature, title compound (B-8) was obtained by RP-HPLC (C18, acetonitrile /water containing 0.1 % of trifluoroacetic acid as eluant) as its trifluoroacetate salt.

¹H NMR (DMSO-d₆, 600 MHz) δ 13.42 (bs, 1 H), 12.34 (s, 1 H), 10.06 (bs, 1 H), 9.64 (t, *J*=5.9 Hz, 1 H), 7.52 (s, 5 H), 7.43 (dd, *J*=8.4 Hz, *J*=5.6 Hz, 2 H), 7.23 (t, *J*=8.8 Hz, 2 H), 5.28 (s, 1 H), 4.67 (dd, *J*=15.4 Hz, *J*=6.6 Hz, 1 H), 4.59 (dd, *J*=15.5 Hz, *J*=6.0 Hz, 1 H), 3.02 (s, 3 H), 2.06 (s, 3 H).

 13 C NMR (DMSO-d₆, 600 MHz) δ 168.25, 161.32 (d, J=242.9 Hz), 148.41, 144.29, 134.30, 130.89, 130.61, 129.40, 129.24, 129.00 (d, J=8.2 Hz), 125.95, 115.56 (d,

J=21.4 Hz), 68.90, 43.30, 41.20, 40.80.

MS m/z 397 (M+H)⁺.

EXAMPLE 4

30 2-[1-(Dimethylamino)-1-methylethyl]-*N*-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide

Step 1: Benzyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethyl carbamate (C-2)

A methanol solution of methyl 2-(1-{[(benzyloxy)carbonyl]amino}-1-methylethyl)-5,6-dihydroxypyrimidine-4-carboxylate (C-1) (prepared from N-[(benzyloxy)carbonyl]-2-methylalanine by procedures similar to those set forth in Scheme A) was treated with 2 eq. of 4-fluorobenzylamine and refluxed overnight. After evaporation of the solvent, the residue was poured into EtOAc and extracted with 1N HCl and brine. The organic phase was dried over Na₂SO₄, filtered and concentrated under vacuum. The solid residue was triturated with diethyl ether to give

 1 H NMR (DMSO-d₆, 400 MHz) δ 12.4 (bs, 1 H), 12.3 (bs, 1 H), 9.2 (bs, 1 H) 7.5-7.25 (m, 7 H), 7.16 (t, J=8.8 Hz, 2 H), 4.97 (s, 2 H), 4.48 (d, J=6.4 Hz, 2 H), 1.51 (s, 6 H).

Step 2: 2-(1-Amino-1-methylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide(C-3).

the product (C-2).

To a solution of benzyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate (C-2) in methanol 10% Pd/C (10% by weight) was added. The flask was evacuated, then filled with hydrogen and stirred under an hydrogen atmosphere at room temperature for 1 h. The catalyst was filtered off, washed with methanol, the filtrate was evaporated to dryness and the residue was triturated with Et₂O to obtain (C-3) as a pale yellow solid.

¹H NMR (DMSO-d₆, 400 MHz) δ 7.36 (t, J=8.2 Hz, 2 H), 7.16 (t, J=8.8 Hz, 2 H), 4.46 (d, J=6.2 Hz, 2 H), 1.43 (s, 6 H).

10 <u>Step 3</u>: 2-[1-(Dimethylamino)-1-methylethyl]-*N*-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (C-4).

To a stirred solution of (C-3) in methanol about 11 eq. of acetic acid were added and subsequently NaBH₃CN (8 eq.) and formaldehyde (37% solution, 2.5 eq.). The mixture was stirred at room temperature for 5 days, concentrated by rotary evaporation and subjected to RP-HPLC (C18, water/acetonitrile with 0.1% of trifluoroacetic acid as eluant). Collection and liophilization of appropriate fractions afforded the product (C-4) as its trifluoroacetate salt. The white powder was dissolved in 1N HCl and lyophilized again to be converted into the corresponding hydrochloride salt.

¹H NMR (DMSO-d₆, 300 MHz) δ 12.4 (s, 1 H) 10.2 (bs, 2 H), 7.41 (dd, J =8.3 Hz, J =6.9 Hz, 2 H), 7.16 (t, J=8.3 Hz, 2 H), 4.50 (d, J =5.9 Hz, 2 H), 2.73 (s, 6 H), 1.60 (s, 6 H). MS m/z 349 (M+H)⁺.

25 EXAMPLE 5

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N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylmorpholin-3-yl)-pyrimidine-4-carboxamide

Step 1: 4-(tert-butoxycarbonyl)morpholine-3-carboxylic acid (C-5).

To a vigorously stirred solution of 3-morpholinecarboxylic acid and triethylamine (1.11 eq.) in MeOH at 50 °C was added di-t-butyl dicarbonate (2 eq.). Stirring was continued at 50 °C for 5 min and at room temperature overnight. The reaction mixture was then concentrated to obtain an oily residue and suspended between EtOAc and saturated NaHCO₃. The organic layer was extracted with saturated NaHCO₃ and H₂O. The combined aqueous layers were brought to pH = 2.0 with 3 M HCl and immediately extracted with EtOAc. The combined organic layers were washed with dilute HCl, dried, filtered and evaporated to give C-5 as a pale yellow oil, a 1:1 mixture of rotamers by NMR. δ ¹H NMR (400 MHz, DMSO-d6) 12.93 (bs, 1 H), 4.32 (s, 0.5 H), 4.29 (s, 0.5 H), 4.2-4.1 (m, 1 H), 3.83-3.74 (m,1 H), 3.58-3.52 (m, 2 H), 3.36-3.31 (m, 1 H), 3.16 (t, J=11.4 Hz, 0.5 H), 3.00 (t, J=11.4 Hz, 0.5 H), 1.40 (s, 4.5 H), 1.36 (s, 4.5 H). MS m/z 232 (M+H)⁺.

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Step 2: tert-Butyl 3-(aminocarbonyl)morpholine-4-carboxylate-(C-6).

To a stirred solution of compound C-5 (1 eq.), pyridine (0.6 eq.) and di-t-butyl dicarbonate (1.3 eq.) in dioxane, NH₄HCO₃ (1.26 eq.) was added and the mixture was stirred at room temperature for 20 hours. Mixture was concentrated, taken up in EtOAc and washed with water and brine. Organics were dried over Na₂SO₄ and evaporated giving C-6 as an oil which crystallized at room temperature. ¹H-NMR (DMSO-d₆, 300 MHz) δ 7.35 (bs, 1 H), 7.06 (bs, 1 H), 4.15 (bs, 2 H), 3.76 (bs, 1 H), 3.57-3.51 (m, 2 H), 3.28 (m, 1 H), 3.18 (m, 1 H), 1.36 (s, 9 H).

MS m/z 231 (M+H)⁺.

Step 3:

tert-Butyl 3-cyanomorpholine-4-carboxylate-(C-7).

A solution of C-6 (1 eq.) and triethylamine (2.1 eq.) in CH₂Cl₂ was cooled to 0°C and trifluoroacetic anhydride (1.1 eq.) added dropwise under nitrogen. Stirring was continued 3.5 hours more at room temperature and volatiles removed in vacuo. Residues taken in EtOAc were washed with water, brine and dried over Na₂SO₄. Evaporation gave the title compound as a brown solid.

¹H NMR (DMSO-d₆, 400 MHz) δ 5.04 (d, J = 2.7 Hz, 1 H), 3.96 (d, J=12.2 Hz, 1 H), 3.86 (dd, J= 11.5, 2.6 Hz, 1 H), 3.69 (d, J=12.4 Hz, 1 H), 3.56 (dd, J = 12.2, 3.2 Hz, 1 H), 3.40 (td, J = 11.9, 2.89 Hz, 1 H), 2.97 (m, 1 H), 1.43 (s, 9 H). MS m/z 213 (M+H)⁺.

15 <u>Step 4</u>: tert-Butyl 3-[(Z)-amino(hydroxyimino)methyl]morpholine-4-carboxylate- (C-8).

A solution of C-7 (1 eq.), hydroxylamine hydrochloride (1.4 eq.) and triethylamine (1.7 eq.) in EtOH was refluxed under nitrogen for 5 hours. Mixture was concentrated and residues taken up in EtOAc and washed with water and brine. Combined organics were dried over Na₂SO₄ and evaporated giving C-8 as yellow solid.

¹H NMR (DMSO-d₆, 400 MHz) δ 9.16 (bs, 1 H), 5.32 (bs, 2 H), 4.30 (bs, 1 H), 4.08 (d, J=11.6 Hz, 1 H), 3.75 (d, J = 6.8 Hz, 1 H), 3.50-3.33 (m, 4 H), 1.38 (s, 9 H) MS: m/z 246 (M+H)⁺.

5 <u>Step 5</u>: Dimethyl-2-({2-amino-2-[4-(*tert*-butoxycarbonyl)morpholin-3-yl]ethenyl}oxy)but-2-enedioate- (**C-9**).

O COOMe

$$NH_2$$
 COOMe

 NH_2 COOMe

 NH_2 COOMe

A solution of C-8 (1 eq.) and dimethylacetylenedicarboxylate (1.2 eq.) in CHCl₃ was refluxed for 1 hour under nitrogen and solution concentrated. Residue was purified by flash chromatography on silica gel, eluents petroleum ether/EtOAc 7:3 -> 1:1, to give the desired product as a mixture of two isomers E/Z (76:14).

¹H NMR (DMSO-d₆, 400 MHz, 300K) δ 6.60 and 6.20 (2 bs, 2 H), 5.58 and 5.41 (2s, 1 H), 4.36 (bs, 1 H), 4.04 (bs, 1 H), 3.8 (bs, 1 H), 3.76 and 3.72 (2 s, 3 H), 3.63 and 3.58 (2 s, 3 H), 3.53 (td, J = 13.6, 3.7 Hz, 1 H), 3.44 (t, J = 10.4 Hz, 1 H), 3.31 (m, 2 H), (s, 9 H). MS m/z 388 (M+H)⁺.

Step 6: tert-Butyl-3-[4,5-dihydroxy-6-(methoxycarbonyl)pyrimidin-2-yl]morpholine-4-carboxylate-(C-10).

The adducts C-9 were refluxed in xylenes for 24 hours. Then the reaction was cooled and concentrated in vacuo. Ethyl ether was added until precipitation of a solid that was filtered, washed with ethyl ether and dried to give the pyrimidine C-10 as an orange solid.

- ¹H NMR (DMSO-d₆, 400 MHz, 340 K) δ 4.62 (s, 1H), 4.15 (d, J =12 Hz, 1H), 3.84 (bs,1H), 3.82 (s, 3H), 3.70 (dd, J = 12.3, 4 Hz, 1H), 3.61 (dd, J= 12.2, 3.8 Hz, 1H), 3.56 (t, J= 13 Hz, 1H), 3.43 (td, J= 11.5, 3.4 Hz, 1H), 1.35 (s, 9H).
 MS m/z 356 (M + H)⁺.
- 10 Step 7: Methyl 5,6-dihydroxy-2-morpholin-3-ylpyrimidine-4-carboxylate (C-11).

The methyl ester A was treated with a mixture of TFA:dichloromethane:H₂O (65:35:10) at room temperature for 15 minutes. The reaction mixture was concentrated and the residue was taken up in Et₂O and expressed several times in order to remove excess trifluoroacetic acid. A solid

evaporated several times in order to remove excess trifluoroacetic acid. A solid residue was obtained after filtration.

¹H NMR (DMSO-d₆, 400 MHz, 300K) δ 13.24 (bs, 1 H), 10.54 (bs, 1H), 9.54 (bs, 2H), 4.34 (d, J= 6.9 Hz, 1 H), 4.24 (dd, J = 12.2, 3.2 Hz, 1H), 3.93 (d, J = 11.2 Hz, 1H), 3.84 (s, 3H), 3.75 (t, J= 10.3 Hz, 1H), 3.58 (t, J= 10.5 Hz, 1H), 3.32 (d, J=12.8)

Hz, 1H), 3.20 (td, J = 11, 3.7 Hz, 1H).

MS: m/z 256 (M+H)⁺.

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Step 8: N-(4-fluorobenzyl)-5,6-dihydroxy-2-morpholin-3-ylpyrimidine-4-carboxamide (C-12).

The methyl ester C-11 in dry MeOH was treated with 4-fluorobenzyl amine (2.0 eq.) at 90 °C for 1 hour. The reaction mixture was concentrated and the residue triturated with Et₂O. A solid residue was obtained. Title compound was isolated by RP-HPLC as its trifluoroacetate salt (C18 column, eluants water/acetonitrile containing 0.1 % TFA).

¹H NMR (DMSO-d₆ + TFA, 400 MHz, 300 K) δ 9.63 (bs, 1 H), 9.4 (t, *J*=6.07 Hz, 1 H), 9.2 (bs, 1 H), 7.39 (dd, *J*=8.31, *J*=5.76 Hz, 2 H), 7.18 (t, *J*= 8.84 Hz, 2 H), 4.59 (dd, *J*=15.53, *J*=6.80 Hz, 1 H), 4.53 (dd, *J*=15.36, *J*=6.24 Hz, 1 H), 4.37 (bs, 1 H), 4.24 (dd, *J*=12.41, *J*=3.24 Hz, 1 H), 3.99 (d, *J*=12.04 Hz, 1 H), 3.74-3.62 (m, 2 H), 3.41 (d, *J*= 13.09 Hz, 1 H), 3.40 (bs, 1 H).

MS *m/z* 349 (M + H) †.

Step 9: N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylmorpholin-3-yl)-pyrimidine-4-carboxamide (C-13).

To a solution of C-12 (1 eq.) in MeOH were added 37% HCOH (6 eq.), NaBH₃CN (5.2 eq.) and AcONa (5.8 eq.). Mixture was stirred at room temperature under nitrogen for 12 hours, then concentrated and title compound C-13 was obtained by RP-HPLC purification on a C18 column (eluants water/acetonitrile containing 0.1 % TFA) as its trifluoacetate salt.

¹H NMR (DMSO-d₆+TFA, 400 MHz, 330 K) δ 9.2 (bt, 1 H), 7.40 (dd, *J*=8.38, *J*=5.75 Hz, 2 H), 7.16 (t, *J*=8.84 Hz, 2 H), 4.57 (d, *J*=6.34 Hz, 2 H), 4.27 (dd, *J*=10.03, *J*=3.55 Hz, 1 H), 4.22 (dd, *J*=12.82, *J*=3.22 Hz, 1 H), 4.10 (d, *J*=13.73 Hz, 1 H), 3.77 (t, *J*=11.84 Hz, 1 H), 3.65-3.60 (m, 2 H), 3.41 (td, *J*=12.54, *J*=3.67 Hz, 1

25 H), 2.87 (s, 3 H).
MS m/z 363 (M+H)⁺.

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EXAMPLE 6

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpyrrolidin-2-yl)pyrimidine-4-30 carboxamide

Step 1: Tert-butyl-2-[amino(hydroxyimino)methyl]pyrrolidine-1-carboxylate (C-14).

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A solution of hydroxylamine hydrochloride (1.0 eq.) in MeOH was added at 0 °C to a solution of KOH (1.0 eq.) in MeOH. The resulting reaction mixture was filtered and added to a solution of *tert*-butyl-2-cyanopyrrolidine-1-carboxylate (1.0 eq.) in methanol and stirred at 40 °C for 2 h. The solvent was removed *in vacuo* and the residue treated with water, the solid was filtered and washed with a mixture of Et₂O: Petroleum Ether 1:1 to afford the title compound C-14 as a white solid.

¹H-NMR (DMSO- d_6 , 400 MHz) δ 8.92 (s, 1 H), 5.35 (s,1 H), 5.15 (s, 1 H), 4.25 (bs, 0.5 H), 4.10 (s, 0.5 H), 3.40-3.30 (m, 1 H), 2.10-1-70 (m, 4 H), 1.40 (s, 4.5 H),1.35 (s, 4.5 H), one signal is obscured by water.

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Step 2: Methyl 5-(benzoyloxy)-2-[1-(tert-butoxycarbonyl)pyrrolidin-2-yl]-6-hydroxypyrimidine-4-carboxylate (C-15).

A solution of C-14 (1.0 eq.) and dimethyl acetylenedicarboxylate (1.05 eq.) in CHCl₃ was refluxed for 3 h. The reaction mixture was concentrated and the crude product was used directly in the next step without further purification. The crude product was dissolved in xylene and refluxed for 24 h. The solvent was removed in vacuo and the crude was dissolved in pyridine. Benzoic anhydride was added (1.5 eq.). The reaction mixture was stirred at room temperature until the starting material was consumed as determined by MS analysis. The reaction mixture concentrated, the resulting oil was diluted with ethyl acetate and washed with 1N HCl solution, saturated NaHCO3 solution, brine. The crude oil obtained after organic solvent evaporation was purified by flash chromatography to obtain C-15 as a yellow 10 solid. ¹H-NMR (CDCl₃, 400 MHz) δ 12.08 (bs, 1 H), 8.18 (d, J = 7.6 Hz, 2 H), 7.64 (t, J =7.6 Hz, 1 H), 7.50 (t, J = 7.6 Hz, 2 H), 4.80-4.60 (m, 1 H), 3.82 (s, 3 H), 3.60-3.50 (m, 1 H), 3.40-3.20 (m, 1 H), 2.50-2.10 (m, 2 H), 2.00-1.70 (m, 2 H), 1.50 (s, 9 H). $MS m/z 444 (M+H)^{+}$. 15

Step 3: Methyl 5-(benzoyloxy)-6-hydroxy-2-pyrrolidin-2-ylpyrimidine-4-carboxylate (**C-16**).

Methyl 5-(benzoyloxy)-2-[1-(tert-butoxycarbonyl)pyrrolidin-2-yl]-6-hydroxypyrimidine-4-carboxylate C-15 was treated with TFA:CH₂Cl₂ (3:7) at 0 °C. The solution was warmed to room temperature and the progress of the reaction was monitored by MS analysis. After 1h the reaction was complete and the solvent was removed under reduced pressure using a rotatory evaporator. The product C-16 was precipitated with Et₂O and collected by filtration.

1H NMR (CDCl₃, 400 MHz) δ 8.14 (d, *J*=7.5 Hz, 2 H), 7.67 (t, *J*=7.6 Hz, 1 H), 7.50 (dd, *J*=7.6, 7.6 Hz, 2 H), 4.99 (dd, *J*=14.9, *J*=7.3 Hz, 1 H), 3.78 (s, 3 H), 3.60-3.40 (m, 2 H), 2.60-2.45 (m, 1 H), 2.40-2.30 (m, 1 H), 2.20-2.10 (m, 2 H). MS *m*/z 344 (M+H)⁺.

Step 4:

N-(4-fluorobenzyl)-5,6-dihydroxy-2-pyrrolidin-2-ylpyrimidine-4-carboxamide (C-17).

A solution of methyl 5-(benzoyloxy)-6-hydroxy-2-pyrrolidin-2-ylpyrimidine-4-carboxylate (C-16) (1.0 eq.) in MeOH was treated with 4-fluorobenzylamine (3.0 eq.). The solution was stirred at reflux until the starting material was consumed as determined by MS analysis. The reaction was concentrated and the product (C-17) was precipitated with MeOH and collected by filtration.
10 HNMR (DMSO-d₆, 400 MHz) δ 9.55 (bs, 1 H), 7.35 (dd, J = 13.7, J = 7.8 Hz, 2 H), 7.16 (dd, J=17.5, J=8.8 Hz, 2 H), 4.60-4.40 (m, 2 H), 4.06 (dd, J=14.0, J=6.9 Hz, 1 H), 3.15-3.10 (m, 1 H), 3.00-2.90 (m, 1 H), 2.20-2.10 (m, 1 H), 1.90-1.70 (m, 3 H). MS m/z 333 (M+H)⁺.

15 <u>Step 5</u>: N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpyrrolidin-2-yl)pyrimidine-4-carboxamide (C-18).

To a stirred solution of N-(4-fluorobenzyl)-5,6-dihydroxy-2-pyrrolidin-2-ylpyrimidine-4-carboxamide (C-17) (1.0 eq.) in MeOH, Et₃N (1.0 eq.) was added followed by the addition of AcONa (1.6 eq.), AcOH glacial (1.6 eq.), 37% HCOH (2.0 eq.) and NaBH(AcO)₃ (1.4 eq.). The mixture was stirred at room temperature until the reactants were consumed as determined by MS analysis. The reaction mixture was quenched by adding aqueous NaHCO₃, and the product extracted with EtOAc. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure using a rotatory evaporator. A portion of the mixture was purified by RP-HPLC (C18, water/acetonitrile with 0.1% of trifluoroacetic acid as eluant) to give the title compound C-18 as its trifluoroacetate salt.

¹H NMR δ (DMSO- d_6 , 400 MHz) δ 13.20 (bs, 1 H), 12.50 (bs, 1 H), 10.0-9.70, (m, 1 H), 9.63 (bs, 1 H), 7.35 (dd, J=13.8 Hz, J=8.2 Hz, 2 H), 7.18 (dd, J=17.5 Hz, J=8.8 Hz, 2 H), 4.54 (m, 2 H), 4.40 (dd, J=15.7 Hz, J=7.7 Hz, 1 H), 3.82-3.70 (m, 1 H), 3.40-3.20 (m, 1 H), 2.94 (s, 3 H), 2.60-2.50 (m, 1 H), 2.20-1.80 (m, 3 H). MS m/z 347 (M+H)⁺.

EXAMPLE 7

2-(1,4-dimethylpiperazin-2-yl)-*N*-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide

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Step 1: Preparation of Compound C-20

Compound C-19 (which was prepared from 1-[(benzyloxy)carbonyl]-4-(tert-butoxycarbonyl)piperazine-2-carboxylic acid (Bigge et al, Tetrahedron Lett. 1989, 30: 5193) using procedures similar to those set forth in Scheme A) was deprotected with TFA/dichloromethane 1:1. After 1.5 h the solution was evaporated to obtain the crude product C-20.

Step 2: Preparation of Compound C-21

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To the crude C-20 dissolved in MeOH, NaCNBH₃ (1.4 eq.), AcONa (1.6 eq.) and HCHO 37% (2 eq.) were added. After 1 h the mixture was evaporated to obtain crude C-21.

Step 3: Preparation of Compound C-22

Crude C-21 dissolved in MeOH and hydrogenated at atmospheric pressure on 10% Pd/C overnight. After filtration and evaporation of the filtrate crude C-22 was obtained.

Step 4: Preparation of Compound C-23

$$H_3C$$
 N
 CO_2
 Me
 $C-23$

Crude C-22 was dissolved in MeOH and NaCNBH₃ (1.4 eq.), AcONa (1.6 eq.) and HCHO 37% (2 eq.) were added. After 2.5 h the mixture was evaporated to obtain crude product C-23.

Step 5:

2-(1,4-dimethylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-

dihydroxypyrimidine-4-carboxamide C-24

Crude C-23 was dissolved in NMP (6 ml/mmol) and 4-

fluorobenzylamine (3 eq.) added. The mixture was stirred at 90°C overnight. Part of

the crude material was purified by preparative HPLC (C18, gradient of CH₃CN/H₂O+0.01% TFA) to obtain the title product (C-24) as its trifluoroacetate salt.

 1 H NMR (DMSO d₆+TFA, 300 K, 400 MHz) δ 12.5 (bs, 1 H), 9.30 (t, J=6.4 Hz, 1 H), 7.38 (dd, J= 5.8, 8.8 Hz, 2 H), 7.17 (t, J=8.8 Hz, 2 H), 4.58-4.4 (m, 2 H), 3.66 (bs, 1

10 H), 3.55-3.35 (m, 3 H), 3.20 (d, *J*=13.3 Hz, 1 H), 3.03, (t, *J*=11.7 Hz, 1 H), 2.79 (s, 3 H), 2.85-2.70 (m, 1 H), 2.33 (bs, 3 H).

MS m/z 376 (M+H)⁺.

EXAMPLE 4A

15 2-[4-(dimethylamino)tetrahydro-2*H*-pyran-4-yl]-*N*-[4-fluoro-2-(methylsulfonyl)benzyl]-5,6-dihydroxypyrimidine-4-carboxamide

Step 1:

terr-Butyl 4-(aminocarbonyl)tetrahydro-2H-pyran-4-yl-carbamate (C-25)

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To a stirred solution of the commercially available 4-[(tert-butoxycarbonyl)amino]tetrahydro-2*H*-pyran-4-carboxylic acid in dioxane, pyridine (0.6 eq.), di-butyl dicarbonate (1.3 eq) and ammonium bicarbonate (1.26 eq) were added and the mixture was stirred at room temperature for 20 hours. Dioxane was

concentrated and the residue dissolved in ethyl acetate and washed with HCl 1N, saturated aqueous NaHCO₃ solution and brine, dried over Na₂SO₄, filtered and evaporated in vacuo to obtain the solid compound (C-25).

¹H NMR (CDCl₃, 300 MHz, 300 K) δ 6.82 (bs,1H), 5.37 (bs, 1H), 4.80 (bs, 1H), 3.88 (t, J = 4.4 Hz, 1H), 3.84 (t, J = 4.4 Hz, 1H), 3.72-3.64 (m, 2H), 2.30-2.21 (m, 2H), 1.98-1.94 (m, 2H), 1.48 (s, 9H).

MS: m/z 245 $(M+H)^+$.

Step 2: tert-Butyl 4-cyanotetrahydro-2H-pyran-4-yl-carbamate (C-26)

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A solution of *tert*-butyl 4-(aminocarbonyl)tetrahydro-2H-pyran-4-yl-carbamate (C-25) and triethylamine (2.1 eq.) in dichloromethane was cooled to 0°C and trifluoroacetic anhydride (1.1 eq.) was added dropwise under nitrogen. Stirring was continued for 1 hour allowing the mixture to reach room temperature. Volatiles were removed *in* vacuo and residue was taken up in ethyl acetate, washed with HCl 1N, brine and dried over Na₂SO₄. Evaporation gave a crude which was purified by flash chromatography on silica gel (eluent: petroleum ether : ethyl acetate = 7:3) to give the title compound (C-26), colorless oil, as a 8:2 mixture of two rotamers by ¹H NMR.

¹H NMR (CDCl₃, 300 MHz, 300 K) δ 4.71 (bs, 1H), 3.96 (t, J = 3.5 Hz, 1H), 3.93 (t, J = 4.1 Hz, 1H), 3.79-3.76 (m, 2H), 2.37-2.34 (m, 2H), 1.89-1.82 (m, 2H), 1.50 (s, 7H), 1.47 (s, 2H).

MS: m/z 227 (M+H)⁺.

<u>Step 3</u>:

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tert-Butyl-4-[amino(hydroxyimino)methyl]tetrahydro-2H-pyran-4-yl-

carbamate (C-27)

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A solution of free hydroxylamine in ethanol was obtained by dissolving separately hydroxylamine hydrochloride (1.1 eq) and potassium hydroxide (1.1 eq) in ethanol. The two solutions were mixed together, the potassium chloride filtered off and the resulting ethanolic solution was used to treat a solution of *tert*-butyl-4-cyanotetrahydro-2H-pyran-4-yl-carbamate (C-26) in ethanol at 45 °C for 5 hours. Mixture was concentrated to obtain the title compound (C-27) as a crude solid that was used in the next step without further purification.

MS: m/z 260 (M+H)⁺.

10 <u>Step 4</u>: Dimethyl-2-{[(amino{4-[(tert-butoxycarbonyl)amino]tetrahydro-2H-pyran-4-yl}methylidene)amino]oxy}but-2-enedioate (C-28)

A solution of *tert*-butyl-4-[amino(hydroxyimino)methyl]tetrahydro-2H-pyran-4-yl-carbamate (C-27) and dimethylacetylendicarboxylate (1.2 eq.) in chloroform was refluxed for 1 hour under nitrogen and the solution was concentrated. Residue was purified by flash chromatography on silica gel (eluent: petroleum ether :ethyl acetate = 7:3) to give the desired product (C-28) as a mixture of isomers in ratio 7:3.

¹H-NMR (CDCl₃, 300 MHz, 300 K) δ 5.91 (bs, 1H), 5.83 (s, 0.7H), 5.75 (s, 0.3H), 5.67 (bs, 1H), 4.67 (s, 0.7H), 4.63 (s, 0.3H), 3.93 (s, 2.1H), 3.86 (s,0.9H), 3.84-3.63 (m, 4H), 3.76 (s, 0.9H), 3.73 (s, 2.1H), 2.32-2.17 (m, 2H), 2.14-1.98 (m, 2H), 1.47 (s,

MS: $m/z 402 (M+H)^{+}$.

9H).

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Step 5: Methyl 2-{4-[(tert-butoxycarbonyl)amino]-tetrahydro-2H-pyran-4-yl}-5,6-dihydroxypyrimidine-4-carboxylate (C-29)

OH OH OH BocHN N CO₂Me A solution of dimethyl-2-{[(amino{4-[(tert-butoxycarbonyl)amino]tetrahydro-2*H*-pyran-4-yl}methylidene)amino]oxy}but-2-enedioate (**C-28**) in o-xylene was refluxed for 6 hours. Then the reaction was cooled down and concentrated. Ethyl ether was added until precipitation of a solid that was filtered, washed with other ethyl ether and dried to give the title compound (**C-29**)as a brown solid.

MS: m/z 370 (M+H)⁺.

The reaction mother liquor was concentrated and used for the next step.

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<u>Step 6</u>:

Methyl 5-(benzoyloxy)-2-{4-[(tert-butoxycarbonyl)amino]tetrahydro-2*H*-pyran-4-yl}-6-hydroxypyrimidine-4-carboxylate (**C-30**)

The concentrated mother liquor containing methyl 2-{4-[(tert-

butoxycarbonyl)amino]-tetrahydro-2*H*-pyran-4-yl}-5,6-dihydroxypyrimidine-4-carboxylate (**C-29**), dissolved in dry pyridine was treated with benzoic anhydride (2 eq.) overnight at room temperature.

The mixture was evaporated, taken up in ethyl acetate and washed with HCl 1N and brine. Organics were dried over Na₂SO₄, filtered and evaporated the resulting crude

oil was purified by flash chromatography on silica gel (eluent: ethyl acetate: petroleum ether = 7:3) to obtain methyl 5-(benzoyloxy)-2-{4-[(tert-butoxycarbonyl)amino]tetrahydro-2*H*-pyran-4-yl}-6-hydroxypyrimidine-4-carboxylate (C-30).

 1 H NMR (DMSO-d₆, 300 MHz, 300 K) δ 13.20 (bs, 1H), 8.09 (d, J = 7.3 Hz, 2H),

25 7.79 (t, J = 7.5 Hz, 1H), 7.63 (t, J = 8.01 Hz, 2H), 3.76 (s, 3H), 3.75-3.60 (m, 4H), 2.22-2.15 (m, 2H), 2.00-1.87 (m, 2H), 1.34 (bs, 9H). MS: m/z 474 (M+H)⁺.

Step 7: tert-Butyl-4-[4-({[4-fluoro-2-(methylsulfonyl)benzyl]amino}carbonyl)-5,6-dihydroxypyrimidin-2-yl]tetrahydro-2H-pyran-4-yl-carbamate (C-31)

Methyl-5-(benzoyloxy)-2-{4-[(tert-butoxycarbonyl)amino]tetrahydro-2*H*-pyran-4-yl}-6-hydroxypyrimidine-4-carboxylate (C-30) in dry MeOH was treated with 4-fluoro-2-(methylsulfonyl)benzylamine (2.5 eq.) at reflux for 2 hours. Solvent was removed in vacuo and the residue was taken up in ethyl acetate, washed with HCl 1N, brine, dried over Na₂SO₄. The filtrate was concentrated in vacuo and triturated with ethyl ether to obtain the crude title compound (C-31).

MS: m/z 541 (M+H)+.

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Step 8: 2-(4-Aminotetrahydro-2*H*-pyran-4-yl)-N-[4-fluoro-2-(methylsulfonyl)benzyl]-5,6-dihydroxypyrimidine-4-carboxamide trifluoroacetate (C-32)

A solution of *tert*-butyl-4-[4-({[4-fluoro-2-(methylsulfonyl)benzyl]amino}carbonyl)-5,6-dihydroxypyrimidin-2-yl]tetrahydro-2*H*-pyran-4-yl-carbamate (C-31) in dichloromethane was treated with an excess of trifluoroacetic acid for 3 hours at room temperature. The acid in excess was removed in vacuo to obtain the crude title compound (C-32)as a pale yellow solid, after trituration with ethyl ether.

MS: m/z 441 (M+H)⁺.

Step 9: 2-[4-(dimethylamino)tetrahydro-2H-pyran-4-yl]-*N*-[4-fluoro-2-(methylsulfonyl) benzyl]-5,6-dihydroxypyrimidine-4-carboxamide (C-33)

A solution of 2-(4-aminotetrahydro-2*H*-pyran-4-yl)-N-[4-fluoro-2-(methylsulfonyl)benzyl]-5,6-dihydroxypyrimidine-4-carboxamide trifluoroacetate (C-32) in MeOH was treated with triethylamine (1 eq.), sodium acetate (1.6 eq.), formaldehyde 37% w/w aq. soln. (3 eq.), and sodium cyanoborohydride (1.43 eq.). The mixture was left stirring at room temperature for 1h. Trifluoroacetic acid (3 eq) and sodium cyanoborohydride (0.5 eq) were added, left stirring overnight. The reaction mixture was concentrated and the title compound (C-33)as trifluoro acetate salt was obtained by preparative HPLC purification (C₁₈, eluting with water and acetonitrile containing 0.1 % trifluoroacetic acid in gradient).

¹H NMR (DMSO-d₆+TFA, 300 MHz, 300 K) δ 10.90 (bs, 1H), 9.42 (bt, 1H), 7.76 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 5.6 Hz, 2H), 4.90 (d, J = 6.3 Hz, 2H), 3.93 (d, J = 6.3 Hz, 2H), 3.44 (s, 3H), 3.21-3.06 (m, 4H), 2.72 (s, 6H), 1.90-1.82 (m, 2H). MS: m/z 469(M+H)⁺.

EXAMPLE 6A

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(7-methyl-7-azabicyclo[2.2.1]hept-1-20 yl)pyrimidine-4-carboxamide.

25 <u>Step1</u>: 7-[(benzyloxy)carbonyl]-7-azabicyclo[2.2.1]heptane-1-carboxylic acid (C-35)

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7-benzyl 1-tert-butyl 7-azabicyclo[2.2.1]heptane-1,7-dicarboxylate (C-34)(synthesized following the procedure reported in J.O.C, 1996, 61, 6313-6325) was stirred in TFA/DCM/H₂O (95/5/5, 0.3 M) for 10 minutes. Evaporation of the solvent afforded the titled compound (C-35).

¹H-NMR (DMSOd₆, 300K, 300MHz) δ : 12.5 (bs, 1H), 7.45-7.30 (m, 5H), 5.06 (s, 2H), 4.27 (t, J = 4.6 Hz, 1H), 2.00-1.92 (m, 2H), 1.76-1.65 (m, 4H), 1.55-1.43 (m, 2H). MS (EI+) m/z 276 (M+H)⁺.

Step 2: benzyl 1-(aminocarbonyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate (C-36)

A stirred solution of 7-[(benzyloxy)carbonyl]-7-azabicyclo[2.2.1]heptane-1-carboxylic acid (C-35) in dioxane was treated with pyridine (0.8 eq.) and Boc₂O (1.5 eq.), then ammonium bicarbonate (1.46 eq.) was added and the mixture was stirred at room temperature for 15 hours. Dioxane was concentrated and the residue was taken up in ethyl acetate, washed with HCl 1N and brine and dried over Na₂SO₄ to give, after filtration and concentration, the titled compound (C-36).

¹H-NMR (DMSOd₆, 300K, 300MHz) δ 7.42-7.28 (m, 5H), 7.18 (bs, 1H), 7.00 (bs, 1H), 5.05 (s, 2H), 4.28 (t, J = 4.5 Hz, 1H), 2.00-1.90 (m, 2H), 1.77-1.60 (m, 4H), 1.52-1.40 (m, 2H). MS (EI+) m/z 275 (M+H)⁺.

Step 3: benzyl 1-cyano-7-azabicyclo[2.2.1]heptane-7-carboxylate (C-37)

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Benzyl 1-(aminocarbonyl)-7-azabicyclo[2.2.1]heptane-7-carboxylate (C-36) in dichloromethane was treated at 0 °C with Et₃N (2.1 eq.) and trifluoroacetic anhydride (1.1 eq.) was added dropwise. The reaction mixture was stirred at 0 °C for 30 minutes. Then, it was diluted with dichloromethane, washed with saturated NaHCO₃ solution.

H₂O, brine and dried over Na₂SO₄ Filtration and evaporation afforded the titled compound (C-37).

 1 H-NMR (DMSOd₆, 300K, 300MHz) δ 7.42-7.30 (m, 5H), 5.14 (s, 2H), 4.32 (t, J = 5.0 Hz, 1H), 2.2-1.98 (m, 4H), 1.90-1.70 (m, 2H), 1.62-1.45 (m, 2H). MS (EI+) m/z 257 (M+H)⁺.

Step 4: dimethyl-2-{[(amino{7-[(benzyloxy)carbonyl]-7-azabicyclo[2.2.1]hept-1-yl}methylidene)amino]oxy}but-2-enedioate (C-38).

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Triethyl amine (1.5 eq.), hydroxylamine hydrochloride (1.3 eq.) were added to a solution of benzyl 1-cyano-7-azabicyclo[2.2.1]heptane-7-carboxylate (C-37) in absolute methanol. The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure, the residue was dissolved in chloroform and treated with dimethylacetylene dicarboxylate (2 eq.) for 14 hours at 60 °C.

The reaction mixture was then concentrated and the resulting crude oil was purified

The reaction mixture was then concentrated and the resulting crude oil was purified by flash chromatography (petroleum ether/ EtOAc 1:1) to give the titled compound (C-38) as a mixture of isomers.

¹H-NMR (DMSOd₆, 300K, 300MHz δ: 7.41-7.25 (m, 5H), 6.57 (bs, 1.3 H), 6.17 (bs,0.7 H), 5.66 (s,0.65 H), 5.61 (s, 0.35 H), 5.04 (s, 2H), 4.35-4.30 (m, 1H), 3.79 (s, 1.95H), 3.75 (s, 1.05H), 3.63 (s,1.05H), 3.60 (s,1.95H), 2.15-1.92 (m, 2H), 1.80-1.45 (m, 6H). MS (EI+) m/z 432 (M+H)⁺.

Step 5: benzyl 1-[5-(benzoyloxy)-4-hydroxy-6-(methoxycarbonyl)pyrimidin-2-yl]-7-azabicyclo[2.2.1]heptane-7-carboxylate (C-39)

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Dimethyl-2-{[(amino{7-[(benzyloxy)carbonyl]-7-azabicyclo[2.2.1]hept-1-yl} methylidene) amino]oxy}but-2-enedioate (C-38) was dissolved ortho-xylene and refluxed for 14 hours. Solvent was evaporated after cooling at room temperature and the resulting crude oil was dissolved in pyridine, treated with benzoic anhydride (2 eq.). The reaction mixture was stirred at room temperature for 3 hours. Reaction mixture was concentrated and the residue was taken up in ethyl acetate and washed with HCl 1N and saturated NaHCO₃ solution. The organic phase was dried over Na₂SO₄, filtered and after concentration and purification by flash chromatography the titled compound was obtained.

 1 H-NMR (DMSOd₆, 300K, 300MHz) δ 13.38 (s, 1H), 8.09 (d, J = 7.5 Hz , 2H), 7.80 (t, J = 7.5 Hz , 1H), 7.64 (t, J = 7.5 Hz, 2H), 7.40-7.22 (m, 5H), 5.00 (s, 2H), 4.40 (t, J = 4.3 Hz, 1H), 3.76 (s, 3H), 2.32-1.117 (m, 2H), 1.95-1.79 (m, 4H), 1.66-1.51 (m, 2H). MS (EI+) m/z 504 (M+H)⁺.

Step 6: N-(4-fluorobenzyl)-5,6-dihydroxy-2-(7-methyl-7-azabicyclo[2.2.1]hept-1-yl)pyrimidine-4-carboxamide (C-40)

20 Benzyl 1- [5-(benzoyloxy) -4- hydroxy -6- (methoxycarbonyl) pyrimidin -2- yl] -7- azabicyclo[2.2.1]heptane-7-carboxylate (C-39) in methanol was hydrogenated under H₂ atmosphere in presence of Pd/C 10% (10%w/w) at room temperature for 2 hours. After filtration and evaporation, the crude was dissolved in MeOH and p-fluorobenzylamine (3.5 eq.) added. After being refluxed overnight, the residue was washed with Et₂O/EP. The solid was dissolved in MeOH and NaCNBH₃ (1.4 eq.), AcONa (1.6 eq.), HCHO 37 % (1 eq.) were added. The reaction mixture was stirred at room temperature overnight. The product was purified by preparative HPLC (C18,

gradient $CH_3CN/H_2O + 0.01$ %TFA) to obtaine the title compound (C-40) as trifluoro acetate salt.

¹H-NMR (DMSOd₆, 300K, 400MHz) δ 12.9 (bs, 1H), 12.2 (s, 1H), 10.95 (bs, 1H), 9.66 (bs, 1H), 7.47-7.40 (m, 2H), 7.21-7.12 (m, 2H), 4.50 (d, J = 6.0 Hz, 2H), 4.17 (bs, 1H), 2.67 (s, 3H), 2.45-2.1 (m, 6H), 1.95-1.80 (m, 2H). MS (EI+) m/z 373 (M+H)⁺.

EXAMPLE 7B

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1,2,4-trimethylpiperazin-2-yl)pyrimidine-4-carboxamide.

Step1:

1-benzyl 4-tert-butyl 2-cyano-2-methylpiperazine-1,4-dicarboxylate (C-41).

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To a cooled (-75 °C) solution of LDA 2M in heptane/THF (1.5 eq) in THF, a solution of 1-[(benzyloxy)carbonyl]-4-(tert-butoxycarbonyl)piperazine-2-carboxylic acid (Bigge et al, Tetrahedron Lett. 1989, 30: 5193) in THF was added dropwise at -75 °C. After being stirred for 1 hour at -75 °C, MeI (1.5 eq) was added. After 2 hours at -75 °C the reaction mixture was left warming to r.t., evaporated, diluted with AcOEt, washed with NaHCO₃, water, brine and dried over Na₂SO₄. The crude was purified by flash chromatography on silica gel (petroleum ether/AcOEt, 85:15) to obtain the title compound (C-41).

¹H NMR (DMSOd₆, 340K, 300MHz) δ 7.45-7.30 (m, 5H), 5.19 (AA' system, J = 13 Hz, 2H), 4.05 (d, J = 14 Hz, 1H), 3.87-3.78 (m, 1H), 3.66 (d, J = 14 Hz, 1H), 3.62-3.35 (m, 3H), 1.66 (s, 3H), 1.45 (s, 9H). MS (EI+) m/z 360 (M+H)⁺.

Step 2:

1-benzyl 4-tert-butyl 2-[(Z)-amino({[(1E)-3-methoxy-1-(methoxycarbonyl)-3-oxoprop-1-enyl]oxy}imino)methyl]-2-methylpiperazine-1,4-dicarboxylate (C-42).

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A solution of 1-benzyl 4-tert-butyl 2-cyano-2-methylpiperazine-1,4-dicarboxylate (C-41) in EtOH was added to a solution of Et₃N (3.2 eq) and NH₂OH HCl (3 eq) in EtOH. The mixture was stirred 2 hr at 40 °C. After evaporation of the solvent, the residue was diluted with AcOEt, washed with water, dried over Na₂SO₄, filtered and concentrated. The residue was further dissolved in chloroform and dimethylacetylenedicarboxylate (1.5 eq) added to the stirred solution. Reaction was refluxed over night. The mixture was evaporated and the residue was purified by flash chromatography on silica gel (petroleum ether/AcOEt, 65:35) affording (C-42). ¹H NMR (DMSOd₆, 340K, 300MHz). Two sets of signals were observed due to the presence of the geometric isomers: δ 7.48-7.25 (m, 5H), 6.31, 6.01 (bs, 2H), 5.63, 5.55 (s, 1H), 5.12-5.02 (m, 2H), 3.85-3.60 (m, 9H, at 3.79, 3.76 (s), at 3.66, 3.61 (s)), 3.60-3.45 (m, 2H), 3.45-3.31 (m, 1H), 1.51, 1.45 (s, 3H), 1.41 (s, 9H). MS (EI+) m/z 535 (M+H)⁺.

20 <u>Step3</u>: 1-benzyl 4-*tert*-butyl 2-[5-(benzoyloxy)-4-hydroxy-6-(methoxycarbonyl) pyrimidin-2-yl]-2-methylpiperazine-1,4-dicarboxylate (C-43)

25 1-benzyl 4-tert-butyl 2-[(Z)-amino({[(1E)-3-methoxy-1-(methoxycarbonyl)-3-oxoprop-1-enyl]oxy}imino)methyl]-2-methylpiperazine-1,4-dicarboxylate (C-42) was dissolved in xylene and stirred at 155 °C for 8h. After evaporation of the solvent,

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the residue was dissolved in pyridine and benzoic anhydride (1.5 eq) was added. The reaction mixture was stirred at room temperature over night, then pyridine was evaporated. The residue was diluted with AcOEt, the organic phase washed with HCl 1N, dried (Na₂SO₄) and evaporated. The product (C-43) was purified by flash

chromatography (eluent: petroleum ether/AcOEt 70/30). 1 H-NMR (DMSOd₆, 340K, 400MHz) δ 12.96 (bs, 1H), 8.11-8.04 (m, 2H), 7.79-7.73 (m, 1H), 7.66-7.58 (m, 2H), 7.37-7.22 (m, 5H), 5.03 (s, 2H), 4.00-3.91 (m, 1H), 3.80-3.52 (m, 7H, at 3.75 (s)), 3.47-3.40 (m, 1H), 1.65 (s, 3H), 1.35 (s, 9H). MS (EI+) m/z 607 (M+H)⁺.

10 Step 4: Methyl 5-(benzoyloxy)-2-[4-(tert-butoxycarbonyl)-2-methylpiperazin-2-yl]-6-hydroxypyrimidine-4-carboxylate (C-44).

1-benzyl 4-tert-butyl 2-[5-(benzoyloxy)-4-hydroxy-6-(methoxycarbonyl)pyrimidin-2-yl]-2-methylpiperazine-1,4-dicarboxylate (C-43) was dissolved in AcOEt and

hydrogenated at 1 atm on 10% (w/w) Pd/C over night. After filtration of the catalyst, solvent was evaporated to give the crude title compound (C-44).
 ¹H-NMR (DMSOd6 + TFA, 340K, 400MHz) δ: 8.11-8.04 (m, 2H), 7.81-7.74 (m, 1H), 7.66-7.58 (m, 2H), 4.22 (d, J = 14.4 Hz, 1H), 3.80 (s, 3H), 3.75-3.67 (m, 2H),

3.63-3.44 (m, 2H), 3.32-3.24 (m, 1H) 1.68 (s, 3H), 1.38 (s, 9H).

20 MS (EI+) m/z 473 (M+H)⁺.

Step 5: methyl 2-[4-(tert-butoxycarbonyl)-1,2-dimethylpiperazin-2-yl]-5,6-dihydroxypyrimidine-4-carboxylate (C-45)

Crude material methyl 5-(benzoyloxy)-2-[4-(tert-butoxycarbonyl)-2-methylpiperazin-25 2-yl]-6-hydroxypyrimidine-4-carboxylate (C-44) obtained in step 1 was dissolved in MeOH, and NaCNBH₃ (2.8 eq), AcONa (3.2 eq) and HCHO (37 % in H₂O, 4eq)

were added. The reaction mixture was stirred at room temperature. After 30', the solvent was evaporated and the crude solid (C-45) obtained washed with Et_2O . MS (EI+) m/z 383 (M+H)⁺.

Step 6:

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tert-butyl 3-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-3,4-dimethylpiperazine-1-carboxylate (C-

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Crude material obtained methyl 2-[4-(tert-butoxycarbonyl)-1,2-dimethylpiperazin-2-yl]-5,6-dihydroxypyrimidine-4-carboxylate (C-45) was dissolved in MeOH and p-fluorobenzylamine (5.0 eq) was added. The mixture was refluxed till the consumption of the starting material was completed; then solvent was evaporated and the crude solid (C-46) obtained washed with Et₂O.

Step 7:

MS (EI+) m/z 476 (M+H)⁺.

2-(1,2-dimethylpiperazin-2-yl)-*N*-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (**C-47**)

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Crude material *tert*-butyl 3-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-3,4-dimethylpiperazine-1-carboxylate (C-46) was stirred in DCM/TFA (1:1) for 1 hour. Evaporation of the solvent afforded the crude title compound (C-47).

MS (EI+) m/z 376 (M+H)⁺.

Step 8: N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1,2,4-trimethylpiperazin-2-yl)pyrimidine-4-carboxamide hydrochloride (C-48) (6).

Crude material obtained in step 2-(1,2-dimethylpiperazin-2-yl)-N-(4-fluorobenzyl)5,6-dihydroxypyrimidine-4-carboxamide (C-47) was dissolved MeOH and Et₃N (2.2 eq) was added. Then NaCNBH3 (2.8 eq), AcONa (3.2 eq) and HCHO (37 % in H₂O, 4eq) were added. The reaction mixture was stirred at room temperature over night.

The reaction mixture was evaporated and the residue purified by preparative HPLC (C18, gradient of $CH_3CN/H_2O + 0.01\%$ TFA) to give the title product (C-48) as trifluoroacetate salt.

 1 H-NMR (CD₃CN + TFA, 280K, 600MHz) δ: 7.50-7.38 (m, 2H), 7.13-7.07 (m, 2H), 4.66-4.51 (m, 2H), 4.00-3.72 (m, 4.3H), 3.60-3.56 (t, J=12.7 Hz, 0.7 H), 3.49-3.44 (t, J=15.5 Hz, 1 H), 3.04 (s, 2H), 2.91 (s, 1H), 2.73 (s, 1H), 2.69 (s b, 2H), 2.05 (s,1H) 1.95 (2H obscured by solvent). MS (EI+) m/z 390 (M+H) $^{+}$.

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EXAMPLE 8

N-(4-Fluorobenzyl)-5,6-dihydroxy-2-(1-methylpiperidin-2-yl)pyrimidine-4-carboxamide (D-2)

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Methyl 5-(benzoyloxy)-6-hydroxy-2-piperidin-2-ylpyrimidine-4-carboxylate (**D-1**)(prepared from 1-[(benzyloxy)carbonyl)]piperidine-2-carboxylic acid by procedures similar to those set forth in Scheme A) was dissolved in the minimal amount of chloroform. To the stirred solution were added tetrahydrofuran, triethylamine (5 eq.) and methyl iodide (3 eq.), and the reaction was stirred at 40 °C. After 30 min, triethylamine (3 eq.) and methyl iodide (2 eq.) were added and mixture was stirred for 30 min at 40 °C. After evaporation of volatiles, the residue was taken up into *N*-methylpyrrolidinone and treated with 3 eq. of 4-fluorobenzylamine at 95 °C for 15 min. The title product (**D-2**) was isolated as its trifluroacetate salt by RP-HPLC (C18, water/acetonitrile with 0.1% of trifluoroacetic acid as eluant).

¹H NMR (DMSO d₆, 400 MHz) δ 13.1 (bs, 1 H), 12.2 (s, 1 H), 9.45 (bs, 1 H), 9.34 (t, J=6.4 Hz, 1 H), 7.37 (dd, J=5.6 Hz, J=8.4 Hz, 2 H), 7.18 (t, J=8.8 Hz, 2 H), 4.57 (d, J=6.4 Hz, 2 H), 4.05 (bs, 1 H), 3.61 (bd, J= 12.4 Hz, 1 H), 3.52-3.50 (m, 1 H), 2.78 (bs, 3 H), 2.16 (d, J= 13.6 Hz, 1 H), 1.92-1.80 (m, 2 H), 1.65-1.46 (m, 3 H). MS m/z 361 (M+H)⁺.

EXAMPLE 9

N-(4-Fluorobenzyl)-5,6-dihydroxy-2-(morpholin-4-ylmethyl)pyrimidine-4-carboxamide

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<u>Step 1</u>:

2-(Diethoxymethyl)-*N*-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (E-2).

To a solution of methyl 2-(diethoxymethyl)-5,6-dihydroxypyrimidine4-carboxylate E-1 (prepared from diethoxyacetonitrile by procedures similar to those set forth in Scheme A) (1.0 eq.) in dry MeOH was added 4-F-benzylamine (3 eq.), stirring at reflux overnight. Solvent was removed in vacuo and the solid residue washed with Et₂O and dried. This material dissolved in CHCl₃ was washed with 2N HCl, brine and dried over Na₂SO₄. Evaporation of solvents gave E-2 as a brown powder.

 1 H NMR (300 MHz, DMSO-d₆) δ 12.62 (bs, 1 H), 12.51 (bs, 1 H), 9.22 (t, J=6.2 Hz, 1 H), 7.36 (dd, J=8.5, 5.7 Hz, 2 H), 7.14 (t, J= 8.9 Hz, 2 H), 5.12 (s, 1 H), 4.45 (d, J=6.3 Hz, 2 H), 3.71-3.41 (m, 4 H), 1.15 (t, J=7.0 Hz, 6 H). MS m/z 366 (M+H)⁺.

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Step 2: N-(4-Fluorobenzyl)-2-formyl-5,6-dihydroxypyrimidine-4-carboxamide (E-3).

A solution of E-2 in 100% formic acid was stirred at 50 °C for 1.5 hours. Volatiles were removed in vacuo and solid residue triturated with Et₂O obtaining after drying E-3 as a white solid.

¹H NMR (300 MHz, DMSO) δ 13.19 (bs, 2 H), 9.62 (t, *J*=6.3 Hz, 1 H), 9.41 (s, 1 H), 7.40 (dd, *J*= 8.5, 5.7 Hz, 2 H), 7.17 (t, *J*=8.8 Hz, 2 H), 4.49 (d, *J*=6.4 Hz, 2 H). MS m/z 292 (M+H)⁺.

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Step 3: N-(4-Fluorobenzyl)-5,6-dihydroxy-2-(morpholin-4-ylmethyl)pyrimidine-4-carboxamide (E-4).

To a solution of E-3 in dry dichloroethane was added morpholine (1 eq.), stirring at room temperature for 30 minutes. NaB(OAc)₃H (1.4 eq.) was added and the reaction stirred at room temperature one more hour. Volatiles were removed in vacuo and solid residue purified by RP-HPLC on a C18 column, eluents water/acetonitrile + 0.1 % TFA, to give E-4 as its trifluoroacetate salt.

¹H NMR (300 MHz, DMSO-d6, 330 K) δ 9.05 (bt, 1 H), 7.38 (dd, J= 8.5, 5.6 Hz, 2 H), 7.15 (t, J = 8.8 Hz, 2 H), 4.51 (d, J=6.3 Hz, 2 H), 3.85 (bs, 2 H), 3.74 (t, J = 4.6 Hz, 4 H), 2.98 (bs, 4 H).

MS m/z 363 (M+H)⁺.

EXAMPLE 10

N-(4-Fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide

Step 1:

4,5-Dihydroxy-6-(methoxycarbonyl)pyrimidine-2-carboxylic acid (F-2).

2-Ethoxycarbonyl-4,5-dihydroxy-6-(methoxycarbonyl)pyrimidine (F-

1) [obtained from ethyl amino(hydroxyimino)ethanoate (Branco et al., *Tetrahedron* 1992, 40: 6335) by procedures similar to those set forth in Scheme A] was suspended in dioxane/THF 2:1 and 1N NaOH was added. After 20 min the mixture was acidified with 1N HCl, concentrated and filtered to give F-2.

 1 H NMR (DMSO-d₆, 300 K, 400 MHz) δ 13.10 (bs, 1 H), 11.11 (bs, 1 H), 3.82 (s, 3

15 H).

MS m/z 213 (M-H).

Step 2: Methyl 5,6-dihydroxypyrimidine-4-carboxylate (F-3).

A solution of F-2 in HCl 1N was stirred for 6 hours at 90 °C. The reaction mixture was filtered and the solid washed with HCl 1N. Evaporation of the filtrate afforded F-3 as a solid.

 $^1 H$ NMR (DMSO d₆, 300 K, 400 MHz) δ 7.75 (s, 1 H), 3.82 (s, 3 H).

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Step 3: N-(4-Fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (F-4).

F-3 was dissolved in DMF and 4-fluorobenzylamine (3 eq.) was added.

After 2 hours at 90 °C the mixture was evaporated. The title product F-4 was purified by preparative HPLC (C18, 5μm, gradient of CH₃CN/H₂O + 0.01% TFA).

¹H NMR (DMSO d₆, 300 K, 400 MHz) δ 12.72 (bs, 1 H), 12.54 (bs, 1 H), 9.48 (bs, 1 H), 7.77 (s, 1 H), 7.36 (t, J=8.0 Hz, 2 H), 7.14 (t, J =8.8 Hz, 2 H), 4.43 (d, J=6.3 Hz, 2 H).

MS m/z 262 (M-H).

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EXAMPLE 11

 $2-\{4-[(\{[(2-chlorophenyl)sulfonyl]amino\}carbonyl)amino]thien-3-yl\}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4 carboxamide$

Step 1:

Methyl 2-{4-[({[(2-chlorophenyl)sulfonyl]amino}carbonyl)amino}-thien-3-yl}-N-(2,3-dimethoxybenzyl) -5,6-dihydroxypyrimidine-4 carboxylate (G-2).

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A solution of methyl 2-(4-aminothien-3-yl)5,6-dihydroxypyrimidine-4-carboxylate trifluoroacetate (1 eq.) G-1 (obtained from the deprotection of the corresponding Boc protected compound) and 2-chlorobenzensulfonylisocyanate (1.02 eq.) in pyridine was stirred at room temperature for 12 h. Pyridine was removed by concentration under reduced pressure. 1N HCl was added to the residue and the resulting solid was collected by filtration. The solid was triturated with H₂O and then Et₂O to give the title compound.

1H NMR (400 MHz, DMSO) δ 13.17 (bs, 1 H), 11.70 (bs, 1 H), 10.91 (bs, 1 H), 10.80 (bs, 1 H), 8.35 (d, J = 3.35 Hz, 1 H), 8.11 (d, J=7.33 Hz, 1 H), 7.77 (m, 2 H), 7.63-7.57 (m, 1 H), 7.58 (d, J=3.35 Hz, 1 H), 3.88 (s, 3 H).

MS m/z 485 (M+H)⁺.

Step 2: 2-{4-[({[(2-chlorophenyl)sulfonyl]amino}carbonyl)amino]thien-3-yl}N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4 carboxamide
(G-3).

A solution of G-2 (1 eq.) and 2,3-dimethoxybenzylamine (1 eq.) in DMF was stirred at 50°C for 12 h. DMF was removed by concentration under reduced pressure. 1N HCl was added to the residue. After filtration a solid was obtained which was triturated with water and then Et₂O. The title product G-3 was obtained by HPLC purification (Nucleosil, gradient: MeCN/H₂O 30%-90% in 10 min) to give the title compound as a solid. 1H NMR (400 MHz, DMSO) δ 13.03 (bs, 1 H), 12.65 (bs, 1 H), 11.60 (bs, 1 H), 9.47 (bs, 1 H), 9.20 (bs, 1 H), 8.11 (d, J = 7.88 Hz, 1 H), 8.05 (m, 1 H), 7.68 (m, 2 H), 7.59

(m, 2 H), 7.07 (app. t, J = 7.94 Hz, 1 H), 6.96 (m, 2 H), 4.57 (s, 1 H), 4.56 (s, 1 H), 3.80 (s, 6 H). MS m/z 620 (M+H)⁺.

EXAMPLE 12

 N^4 -(4-fluorobenzyl)-5,6-dihydroxy- N^2 -(pyridin-2-ylmethyl)pyrimidine-2,4-dicarboxamide

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2-Ethoxycarbonyl-4,5-dihydroxy-6-(methoxycarbonyl)pyrimidine (F-1) was dissolved in DMF and 4-fluorobenzylamine (2.1 eq.) added. After stirring for 10 5 h at 90 °C, a further addition of 4-fluorobenzylamine (0.61 eq.) was done and the mixture was stirred at the same temperature overnight. To this mixture, containing N-(4-fluorobenzyl)-2-ethoxycarbonyl-5,6-dihydroxy-pyrimidine-4-carboxamide (H-2), 2-picolylamine (3 eq.) was added and the reaction was stirred at 90°C for 3 h. The product was purified by preparative RP-HPLC (gradient of $\text{CH}_3\text{CN/H}_2\text{O} + 0.01\%$ 15 TFA), to give the title compound (H-3) as its trifluoroacetate salt 1 H NMR (DMSO-d₆, 300K, 400 MHz) δ 12.90 (bs, 1 H), 12.74 (bs, 1 H), 9.81 (t, J= 6.7 Hz, 1 H), 9.74 (t, J = 6.7 Hz, 1 H), 8.54 (d, J = 4.8 Hz, 1 H), 7.82 (t, J = 6.9 Hz, 1 HzH), 7.40-7.30 (m, 4 H), 7.18 (t, J=8.8 Hz, 2 H), 4.61 (d, J=6.4 Hz, 2 H), 4.56 (d, J=6.4 Hz, 2 H). 20 $MS m/z 398 (M+H)^{+}$.

EXAMPLE 13

2-(1-benzoyl-2,3-dihydro-1*H*-indol-2-yl)-*N*-(4-fluorobenzyl)-5,6-25 dihydroxypyrimidine-4-carboxamide

Step 1: Preparation of Compound I-2

Compound I-1 (prepared from indoline-2-carboxylic acid by protection of the nitrogen and following procedures similar to those set forth in Scheme A) was dissolved in MeOH/EtOAc (1:4) and hydrogenated at atmospheric pressure on 10% Pd/C overnight, crude product I-2 was obtained after filtration and evaporation.

Step 2: Preparation of Compound I-3

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Crude product I-2 was dissolved in THF, followed by pyridine (8 eq.), and PhCOCl (4 eq.). Crude product I-3 was obtained after being stirred at room temperature overnight and solvent evaporation.

Step 3: 2-(1-benzoyl-2,3-dihydro-1*H*-indol-2-yl)-*N*-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (**I-4**).

The crude **I-3** dissolved in DMF and 4-fluorobenzylamine (4 eq.) added. The mixture was stirred at 90°C for 4 hours. The title product **I-4** was purified by preparative RP-HPLC (C18, gradient of CH₃CN/H₂O + 0.01 %TFA).

¹H NMR (DMSO d₆, 340 K, 300 MHz) δ 12.63 (bs, 1 H), 11.92 (bs, 1 H), 8.26 (bs, 1 H), 7.45-6.96 (m, 13 H), 5.38 (dd, J= 4.5 Hz, J= 10.0 Hz, 1H), 4.48-4.36 (m, 2H), 3.60 (dd, J= 10.2 Hz, J= 16.4 Hz, 1 H), 3.19 (dd, J=16.4 Hz, J=4.4 Hz, 1 H). MS m/z 485 (M+H)⁺.

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EXAMPLE 14

N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)-1,2,3,4-tetrahydroquinolin-2-yl]pyrimidine-4-carboxamide

15 <u>Step 1</u>:

Preparation of Compound I-6

The benzoyl protected pyrimidine I-5 [prepared from tetrahydroquinoline-2-carboxylic acid (Robl et al, Tetrahedron Letters, 1995, 36, 1593) by protection of the nitrogen and following procedures similar to those set forth

in Scheme A] was dissolved in EtOAc and hydrogenated at atmospheric pressure on 10% Pd/C at room temperature overnight. **I-6** was obtained after filtration and evaporation of the organic solvent.

5 Step 2: Preparation of Compound I-7

The residue was dissolved in dichloromethane and picolinic acid (1.1 eq.), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.3 eq.), hydroxybenzotriazole (1.3 eq.), and diethylisopropylamine (1.3 eq.) were added. Further additions of the reactants were made until complete consumption of the starting material. Mixture was evaporated to give crude I-7.

Step 3: N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)-1,2,3,4-tetrahydroquinolin-2-yl]pyrimidine-4-carboxamide (I-8)

The crude I-7 product was dissolved in MeOH and 4-fluorobenzylamine (3 eq.) was added. The reaction mixture was refluxed overnight. The product was purified by preparative RP-HPLC (C18 gradient of CH₃CN/H₂O + 0.01% TFA), to give I-8 as its trifluoroacetate salt.

¹H-NMR (DMSO-d₆, 400 MHz, 340 K) δ 12.65 (bs, 1 H), 11.81 (bs, 1 H), 8.37 (d, J = 4.4 Hz, 1 H), 7.92 (bt, 1 H), 7.82 (t, J = 7.0 Hz, 1 H), 7.54 (d, J = 7.6 Hz, 1 H), 7.38

(t, J = 5.4 Hz, 1 H), 7.27 (t, J = 5.4 Hz, 2 H), 7.14-7.10 (m, 3 H), 6.91 (t, J = 6.7, 1 H), 6.70-6.50 (m, 2 H), 5.45 (t, J = 7.2 Hz, 1 H), 4.45-4.35 (m, 2 H), 2.70-2.80 (m, 2 H), 2.05 (bs, 1 H), one proton obscured by DMSO MS m/z 500 (M+H⁺).

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2-Benzyl-N-(4-fluorobenzyl)-5-hydroxy-6-(2-morpholin-4-ylethoxy)pyrimidine-4carboxamide

Methyl 2-benzyl-5-[(tert-butoxycarbonyl)oxy]-6-(2-morpholin-4-Step 1: ylethoxy)pyrimidine-4-carboxylate (N-2)

To a stirred solution of methyl 2-benzyl-5-[(tert-butoxycarbonyl)oxy]-6-hydroxypyrimidine-4-carboxylate (N-1) (prepared from B-5 in Example 3, Step 1 by protection of the 5-hydroxyl group with pivaloyl chloride using a procedure similar to those set forth in Example 6, Step 2) in THF, CsCO₃ (2 eq.) and 4-(2-10 chloroethyl)morpholine (1.5 eq.) hydrochloride were added and mixture reacted at 60 °C for 1 h. Further addition of 4-(2-chloroethyl)morpholine (1 eq.) allowed the complete consumption of starting material after 2 h. The mixture was then allowed to cool to room temperature, poured into EtOAc, extracted with brine, dried (Na₂SO₄),

filtered and concentrated. 15

Step 2: 2-Benzyl-N-(4-fluorobenzyl)-5-hydroxy-6-(2-morpholin-4-ylethoxy)pyrimidine-4-carboxamide (N-3)

The oily residue containing N-2 was taken into DMF and treated with 3 eq. of 4-fluorobenzylamine at 90 °C for 1 h. The title compound (N-3) was isolated as its trifluoroacetate salt by RP-HPLC (C18, water/acetonitrile with 0.1% of TFA as eluant).

¹H NMR (DMSO- d_6 , 400 MHz) δ 12.15 (bs, 1 H), 9.95 (bs, 1 H), 9.75 (t, J=6.4 Hz, 1 H), 7.38 (dd, J=8.5 Hz, J=5.7 Hz, 2 H), 7.34-7.27 (m, 4 H), 7.23-7.14 (m, 3 H), 4.67 (bs, 2 H), 4.49 (d, J=6.4 Hz, 2 H), 4.07 (s, 2 H), 4.00-3.90 (m, 2 H), 3.70-3.40 (m, 6 H), 3.25-3.10 (m, 2 H).

 $MS m/z 467 (M+H^{+}).$

EXAMPLE 16 ·

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-morpholin-4-ylethyl)pyrimidine-4-carboxamide

Step 1:

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To a stirred solution of 2-[1-(dimethylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide hydrochloride (prepared as described in example 4) in NMP an excess of morpholine (10 eq.) was added and mixture was stirred over night at 100 ° C. After cooling to room temperature, title product was isolated by RP HPLC (MeCN/H₂O containing 0.1% TFA as eluant).

¹H NMR (DMSO-d₆) δ 12.33 (bs, 1 H), 9.41 (t, J = 6.0 Hz, 1 H), 7.39 (dd, J = 8.6 Hz, J = 5.5 Hz, 2 H), 7.19 (t, J = 9.1 Hz, 2 H), 4.56 (d, J = 6.0 Hz, 2 H), 3.88 (bs, 2 H),

25 3.29 (bs, 2 H), 1.68 (s, 6 H). MS m/z (M⁺+1) 391

Tables 1 to 25 below list compounds of the present invention which have been prepared. The Tables provide the structure and name of each compound, the mass of its molecular ion plus 1 (M+) or molecular ion minus 1 (M-) as

determined via FIA-MS, and the synthetic scheme employed to prepare the compound. When the compound was prepared as a salt, the identity of the salt is included with the compound name. The synthetic scheme identified as "A*" in the Tables is identical to Scheme A above, except for an additional deprotection step to remove Boc, Cbz, or benzyl present from the substituent in the 2-position of the pyrimidine ring.

Table		·		T
Ехр	Structure	Name	M+	Scheme
1	STATION ON THE PROPERTY OF THE	N-benzyl-5,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide	328	A
2		N-cyclohexyl-5,6-dihydroxy-2-thien 2-ylpyrimidine-4-carboxamide	320	A
3		5,6-dihydroxy-N-(pyridin-2- ylmethyl)-2-thien-2-ylpyrimidine-4- carboxamide (HCl salt)	329	A
4	OH OH FFF	5,6-dihydroxy-2-thien-2-yl-N-[2- (trifluoromethyl)benzyl]pyrimidine- 4-carboxamide	396	A
5	OH OH OH FF	5,6-dihydroxy-2-thien-2-yl-N-[3- (trifluoromethyl)benzyl]pyrimidine- 4-carboxamide	396	A
6	OH OH OH	5,6-dihydroxy-N-(4-methoxybenzył) 2-thien-2-ylpyrimidine-4- carboxamide	358	A
7	OH OH N	N-(2-bromobenzyl)-5,6-dihydroxy-2 thien-2-ylpyrimidine-4-carboxamide	407	A
8	OH OH N	5,6-dihydroxy-N-(pyridin-4- ylmethyl)-2-thien-2-ylpyrimidine-4- carboxamide (HCl salt)	329	A

		27.60	358	A
9	S N OH OH OCH,	5,6-dihydroxy-N-(2-methoxybenzyl) 2-thien-2-ylpyrimidine-4- carboxamide	330	
10	S N H ₃ C O CH ₃	N-(2,6-dimethoxybenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	388	A
11	S N OH OH	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	388	A
12	S N OH OH OH,	5,6-dihydroxy-N-(2-methylbenzyl)- 2-thien-2-ylpyrimidine-4- carboxamide	342	A
13	SHAP OH H ₃ C	N-(2,4-dichloro-6-methylbenzyl)- 5,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide	411	A
14	S N OH N F	N-(2-fluorobenzyl)-5,6-dihydroxy-2- thien-2-ylpyrimidine-4-carboxamide	346	A
15	OH OH FF	5,6-dihydroxy-2-thien-2-yl-N-[4- (trifluoromethyl)benzyl]pyrimidine- 4-carboxamide	396	A
16	S N N N N	N-(1,1'-biphenyl-2-ylmethyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	404	A

	0xy-N-[4-(1.2.3- 412	
17 OH S 5,6-dihydro	0xy-N-[4-(1,2,3- 4-yl)benzyl]-2-thien-2-	A
OH thiadiazol-	ne-4-carboxamide	
s i yipyrimidi	IIG-4-Car GOvernoo]
		i
N-(2.5-dic	hlorobenzyl)-5,6- 397	A
16 dihydroxy	-2-thien-2-ylpyrimidine-4-	
OH carboxami	đe	
		, '
	7.56	
19 OH N-(2-chlor	ro-4-fluorobenzyl)-5,6- 380	A
OH F dihydroxy	-2-thien-2-ylpyrimidine-4	
carboxam	ide	
		•
	ro.4-methylhenzyl)-5.6- 376	A
20 OH N-(3-chlo	10 4 meary 100112-y-/-/-	A
OH dihydroxy	/-2-thien-2-ylpyrimidine-4-	
carboxam	ide	
	chlorobenzyl)-5.6- 397	A
21 OH N-(2,3-di	cmoroccia), o,	A.
LOH \ dihydrox	y-2-thien-2-ylpyrimidine-4-	
s Carboxan	nac	
	brory-2-thien-2-vl-N-[2- 412	
22 он 5,6-dihyd	HOXY-2-UMON 2 / t=	Α.
OH (trifluoro	methoxy)benzyl]pyrimidin	
s e-4-carbo)Xamue	
F-F		
F	1 1	
5 6 dihy	droxy-N-[2- 374	A
23 OH S,0-diffy	hio)benzyl]-2-thien-2-	
vlpyrimi	dine-4-carboxamide	
s N		
l l b HC s		
,,,,		
	droxy-N-(3-phenylprop-2- 352	A
24 OH 5,6-dihy	thien-2-ylpyrimidine-4-	<u></u>
N OH ynyl)-2- carboxa	mide	
S Carboxa		

		5,6-dihydroxy-N-prop-2-ynyl-2-	276	A
25	OH OH	thien-2-ylpyrimidine-4-carboxamide		
	S N N CH			
26	OH OH OH	5,6-dihydroxy-N-(2-hydroxyphenyl) 2-thien-2-ylpyrimidine-4- carboxamide	330	A
27	S N N N N	N-(1-benzofuran-2-ylmethyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	368	A
28	S N N C G	N-(3-chloro-4-fluorobenzyI)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	380	A
29	SHOH OH OH	N-(3,5-dichlorobenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide		A
30	OH H,C O	N-(2,5-dimethoxybenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide	388	A
31	OH OH	N-(2,3-dihydro-1-benzofuran-5- ylmethyl)-5,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide		A
32	2 OH OH CO	N-(2-chloro-6-phenoxybenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4 carboxamide	454	A

		N-(1,2-diphenylethyl)-5,6-	418 T	A
33	QH	dihydroxy-2-thien-2-ylpyrimidine-4		•
- 1	N OH	carboxamide		
	s N	carboxamue	- 1	
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			404	
34	ÇH.	N-(1,1'-biphenyl-3-ylmethyl)-5,6-	404	A
٠.		dihydroxy-2-thien-2-ylpyrimidine-4-	. 1	
		carboxamide	1	
			1	
			ľ	•
		N-(2,3-dimethylbenzyl)-5,6-	356	A
35	ОН	dihydroxy-2-thien-2-ylpyrimidine-4		
		carboxamide		•
	S. C. N. COL	carooxamide		
	W 8 04		- 1	•
36	OH	N-(2-chloro-6-methylbenzyl)-5,6-	376	A
30	OH HIC	dihydroxy-2-thien-2-ylpyrimidine-4-		
		carboxamide	ļ	
	1 LALL		-	
20	7 OH	5,6-dihydroxy-N-(pyridin-3-	329	A
37) Joh	ylmethyl)-2-thien-2-ylpyrimidine-4-		
1	N N	carboxamide (HCl salt)	1	
]	s N			
1			ì	
İ		2 dia 2 di N [3	412	A
3	8 он	5,6-dihydroxy-2-thien-2-yl-N-[3-	412	
	NOH ON	(trifluoromethoxy)benzyl]pyrimidin		
	I . I L M L L	e-4-carboxamide		
1				
l	FF			
1	·	N-[3-fluoro-5-	414	A
				l **
3	9 он Е	N-[3-Hu0ro-3-	i	l
3	9 он Б	(trifluoromethyl)benzyl]-5,6-	ļ	
3		(trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4-		
3		(trifluoromethyl)benzyl]-5,6-		
3		(trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4-		
3		(trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide		A
	S N N F F	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide N-[2-fluoro-5-	414	, A
	S OH F	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide N-[2-fluoro-5-(trifluoromethyl)benzyl]-5,6-	414	, A
	OH F F	(trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide N-[2-fluoro-5- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4-	414	, A
	OH FFF	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide N-[2-fluoro-5-(trifluoromethyl)benzyl]-5,6-	414	, A
	OH FFF	(trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide N-[2-fluoro-5- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4-	414	. A
	OH FFF	(trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide N-[2-fluoro-5- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4-	414	. A

			264	
41	J. OH J.	N-(3,5-difluorobenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	364	A
42	OH OH OH	N-(4-chloro-2-fluorobenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	380	A
43	OH OH CH,	5,6-dihydroxy-N-(3-methoxybenzyl) 2-thien-2-ylpyrimidine-4- carboxamide	358	A
44	S N N F F	N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	414	A
45	SHAPP OH CI	N-(3-chlorobenzyl)-5,6-dihydroxy-2 thien-2-ylpyrimidine-4-carboxamide	362	A
46	OH OH OH	N-(2-chlorobenzyl)-5,6-dihydroxy-2 thien-2-ylpyrimidine-4-carboxamide	362	A
47	OH OH CH,	5,6-dihydroxy-N-(1-phenylpropyl)-: thien-2-ylpyrimidine-4-carboxamide	356	A
48	OH OH OH FF	N-[4-fluoro-3- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-thien-2-ylpyrimidine-4 carboxamide	414	A

49	р н	benzyl 2-{4-	477	A.
	" on on	[(benzylamino)carbonyl]-5,6-	1	
		dihydroxypyrimidin-2-yl}thien-3-	.	
	N. ö	ylcarbamate		
				•
:				
		N-(2,3-dihydro-1H-inden-2-yl)-5,6-	354	A
50	HO, HO		224	Α.
	N COM	dihydroxy-2-thien-2-ylpyrimidine-4-		
	s N	carboxamide		
. 1				•
		N-(3-fluorobenzyl)-5,6-dihydroxy-2-	346	A
51	OH I		540	A
	N OH	thien-2-ylpyrimidine-4-carboxamide	ĺ	
		1	•	
			,	
		E 6 dibudaan N /4 budaan 2	374	
52	ОН	5,6-dihydroxy-N-(4-hydroxy-3-	3/4	A
	NOH OH	methoxybenzyl)-2-thien-2-		
		ylpyrimidine-4-carboxamide	i	
	Ö CH,			
	·	77 (C) A 17 11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	397	
53	. ОН	N-(3,4-dichlorobenzyl)-5,6-	391	A
ļ	N OH O	dihydroxy-2-thien-2-ylpyrimidine-4-		
}		carboxamide		
			j	
		N (4 floorshame) 5 f dibuda and 2	346	A
54	OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	340	A
	N OH F	thien-2-ylpyrimidine-4-carboxamide		
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	ة سا	· 1		
		E C dibudana N /2 simbosani) 0	373	A
55	OH 0 0_	5,6-dihydroxy-N-(3-nitrobenzyl)-2-	1	A
	i i	thien-2-ylpyrimidine-4-carboxamide	· •	_
	N OH			i
		. 1		-
	Ö			
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	OH.	N-(2,4-dichlorobenzyl)-5,6-	397	A
56		dihydroxy-2-thien-2-ylpyrimidine-4-		
		carboxamide		
		Carooxamue		
L				

			364	A
57	OH OH F	N-(3,4-difluorobenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide		
58	SHOH OH OH OH	5,6-dihydroxy-2-thien-2-yl-N-(2,4,6- trimethoxybenzyl)pyrimidine-4- carboxamide	418	A
59	SHOW N	5,6-dihydroxy-N-(1- naphthylmethyl)-2-thien-2- ylpyrimidine-4-carboxamide	378	A
60	CH,	N-(3,4-dimethoxybenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	388	. A
61	OH OH F	N-(2,6-difluorobenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide		A
62	OH OH F	N-(2,5-difluorobenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4 carboxamide	364	A
63	S N N OH	N-(4-chlorobenzyl)-5,6-dihydroxy-thien-2-ylpyrimidine-4-carboxamid	e	A
64	4 OH OH S	N-(2,4-difluorobenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-a carboxamide	364	A

65	SHALL ON THE STATE OF THE STATE	5,6-dihydroxy-2-thien-2-yl-N-(3,4,5- trimethoxybenzyl)pyrimidine-4- carboxamide	418	A
66	OH HCO	N-(3,5-dimethoxybenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	388	A
67	S OH OH OH	5,6-dihydroxy-N-(4-methylbenzyl)- 2-thien-2-ylpyrimidine-4- carboxamide	342	A
68	S N N OH	N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-thien-2-ylpyrimidine-4- carboxamide	372	A
69	S N N S	5,6-dihydroxy-2-thien-2-yl-N-(thien- 2-ylmethyl)pyrimidine-4- carboxamide	334	A
70		N-benzyl-2-[3-({[(2- chlorobenzyl)amino]carbonyl} amino)thien-2-yl]-5,6- dihydroxypyrimidine-4- carboxamide	1- M) 80	A
71	ST N N	N-(2,3-dihydro-1H-inden-1-yl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide	354	A
72	SHOH OH OH	N-[1-(3-furyl)ethyl]-5,6-dihydroxy- 2-thien-2-ylpyrimidine-4- carboxamide	332	A

			000	
73	STATOH TO	N-(1,3-benzodioxol-5-ylmethyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	372	A
74	OH OH N N N N N N N N N N N N N N N N N	5,6-dihydroxy-N-[1-(5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide	349	A
75	S N N N N N N N N N N N N N N N N N N N	5,6-dihydroxy-N-(1,3-thiazol-5- ylmethyl)-2-thien-2-ylpyrimidine-4- carboxamide	335	A
76	OH OH OH OH,	5,6-dihydroxy-N-(2-methoxybenzyl) 2-(5-nitrothien-2-yl)pyrimidine-4- carboxamide	403	A
77	O-N-S-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-	N-benzyl-5,6-dihydroxy-2-(5- nitrothien-2-yl)pyrimidine-4- carboxamide	373	A
78	SHOH OH OH,	N-(3-chloro-4-methylbenzyl)-5,6-dihydroxy-2-(5-nitrothien-2-yl)pyrimidine-4-carboxamide	421	A
79	H,C S N N N	N-benzyl-5,6-dihydroxy-2-(5- methylthien-2-yl)pyrimidine-4- carboxamide	342	A
80	OH OH OH, OH,	N-(2,4-dimethoxybenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4 carboxamide	388	A

			4.4	
81	F. F	N-[3,5-bis(trifluoromethyl)benzyl]-	464	A
31	OH YF	5,6-dihydroxy-2-thien-2-		
ļ	N OH	ylpyrimidine-4-carboxamide	1	
·	s N F		ļ	
l	«∏ N ∏ F/F			
- 1			. 1	
.				
- 00		5,6-dihydroxy-N-(1H-indol-3-	367	A
82	он Г	ylmethyl)-2-thien-2-ylpyrimidine-4-	Į.	
	OH C	carboxamide		
1				
	S N Y			
	Ö			
1				
- 02		N-[1-(2-furyl)ethyl]-5,6-dihydroxy-	332	A
83	ОН	2-thien-2-ylpyrimidine-4-		
	OH _	carboxamide		
	7 >>	Car COAMINGO		
	s N N N			
	() b.,	j !		
84	ÓН	5,6-dihydroxy-N-(isoxazol-3-	319	A
- "	↓ OHO	ylmethyl)-2-thien-2-ylpyrimidine-4-		
ļ	N N N	carboxamide		
	s N	· .		
		<u> </u>		
		5,6-dihydroxy-N-[(4-methyl-1,2,5-	334	A
85	он	5,6-dinydroxy-IN-[(4-nicusy-1,2,5-	334	
- 1	OH NO	oxadiazol-3-yl)methyl]-2-thien-2-		
1		ylpyrimidine-4-carboxamide		· ·
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l	8 Crs			
	· · · ·	5,6-dihydroxy-N-(quinolin-3-	379	A
86	OH N	ylmethyl)-2-thien-2-ylpyrimidine-4-		1
		carboxamide	l l	
			[1
		1	l	1
			204	
87	он	N-(1-benzothien-3-ylmethyl)-5,6-	384	A
	OH S	dihydroxy-2-thien-2-ylpyrimidine-4-	1	1
		carboxamide		
	\			
<u> </u>		5,6-dihydroxy-N-(1H-indol-2-	367	A
88		ylmethyl)-2-thien-2-ylpyrimidine-4-		
	N OH			1
	s h	carboxamide		
		İ	1	
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		7 (12 dimal2	335	A
89	S N N S	5,6-dihydroxy-N-(1,3-thiazol-2- ylmethyl)-2-thien-2-ylpyrimidine-4- carboxamide	333	A
90		5,6-dihydroxy-N-(imidazo[1,2- a]pyridin-2-ylmethyl)-2-thien-2- ylpyrimidine-4-carboxamide	368	A
91	SHOW NOW, NOW,	N-[(1,3-dimethyl-1H-pyrazol-4- yl)methyl]-5,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide	346	A
92	SHOH OH	N-(1-benzothien-2-ylmethyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	384	A
93	STAN TOH	5,6-dihydroxy-N-[(5-phenyl-1,3,4-oxadiazol-2-yl)methyl]-2-thien-2-ylpyrimidine-4-carboxamide	396	A
94	3 1 0 H 0 O O O O O O O O O O O O O O O O O	N-(3-chloro-2-methylbenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	376	A
95	OH CH ₃	N-(5-chloro-2-methylbenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4 carboxamide	376	A
96	S N OH OH OH OH	N-(4-chloro-2-methylbenzyl)-5,6-dihydroxy-2-thien-2-ylpyrimidine-4 carboxamide	376	A

97	OH 7'3	N-(2,5-dimethylbenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	356	A
	O G G		356	
98	STATE OH COL	N-(2,4-dimethylbenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide		
99	OH OH CH,	N-(3,4-dimethylbenzyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	356	A
	8			
100	OH Chiral	N-[(1R)-2,3-dihydro-1H-inden-1-yl] 5,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide	354	A
		N-(2-furylmethyl)-5,6-dihydroxy-2-	318	A
101	SHOH OH	thien-2-ylpyrimidine-4-carboxamide		
102	S N OH OH OH,	5,6-dihydroxy-N-(1-phenylethyl)-2- thien-2-ylpyrimidine-4-carboxamide	342	A
103	N. OH	5,6-dihydroxy-N-[(1S)-1- phenylethyl]-2-thien-2-ylpyrimidine 4-carboxamide	342	A
	l li ou,	_		
104	OH Chiral	5,6-dihydroxy-N-[(1R)-1-phenylethyl]-2-thien-2-ylpytimidine 4-carboxamide	342	A

			206	
105	SHOH OH OH,	methyl 4-({[(5,6-dihydroxy-2-thien- 2-ylpyrimidin-4- yl)carbonyl]amino}methyl)benzoate	386	A
106	OH OH Br	N-(3-bromobenzyl)-5,6-dihydroxy-2 thien-2-ylpyrimidine-4-carboxamide	407	A
107	S N N N Br	N-(4-bromobenzyl)-5,6-dihydroxy-2 thien-2-ylpyrimidine-4-carboxamide	407	A
108	SHOP OH OSCIONS	5,6-dihydroxy-N-[4- (methylsulfonyl)benzyl]-2-thien-2- ylpyrimidine-4-carboxamide	406	A
109	S N OH	5,6-dihydroxy-N-(1,2,3,4- tetrahydronaphthalen-1-yl)-2-thien- 2-ylpyrimidine-4-carboxamide	368	A
110	OH Chiral	N-[(1S)-2,3-dihydro-1H-inden-1-yl]- 5,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide	354	A
111	OH OH FF	5,6-dihydroxy-2-thien-2-yl-N-{[6- (trifluoromethyl)pyridin-3- yl]methyl}pyrimidine-4- carboxamide (HCl salt)	397	A
112	CH OH H ₃ C CH ₃	N-[(1,5-dimethyl-1H-pyrazol-4-yl)methyl]-5,6-dihydroxy-2-thien-2ylpyrimidine-4-carboxamide	346	A

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122	OH NS	5,6-dihydroxy-N-[(2-methyl-1,3- hiazol-4-yl)methyl]-2-thien-2- ylpyrimidine-4-carboxamide (HCl salt)	349	A
123	OH OH	5,6-dihydroxy-N-[(4-phenyl-1,3- thiazol-2-yl)methyl]-2-thien-2- ylpyrimidine-4-carboxamide (HCl salt)	411	A
124	SHOW NOW OH,	5,6-dihydroxy-N-[(5-methyl-1H- 1,2,4-triazol-3-yl)methyl]-2-thien-2- ylpyrimidine-4-carboxamide (HCl salt)	333	A
125	SHAP OH SCH3	5,6-dihydroxy-N-[(4-methyl-1,3- thiazol-2-yl)methyl]-2-thien-2- ylpyrimidine-4-carboxamide (HCl salt)	349	A
126	S N N N	5,6-dihydroxy-N-(6,7,8,9-tetrahydro 5H-benzo[7]annulen-7-ylmethyl)-2- thien-2-ylpyrimidine-4-carboxamide	396	A
127	OH OH N N-CH,	5,6-dihydroxy-N-[(1-methyl-1H- pyrazol-4-yl)methyl]-2-thien-2- ylpyrimidine-4-carboxamide (TFA salt)	332	A
128	ST N S	5,6-dihydroxy-N-[(2-phenyl-1,3-thiazol-4-yl)methyl]-2-thien-2-ylpyrimidine-4-carboxamide (TFA salt)	411	A
129	S N N N N	5,6-dihydroxy-N-(1H-imidazol-2- ylmethyl)-2-thien-2-ylpyrimidine-4- carboxamide (TFA salt)	318	A

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130	STAN	tert-butyl 3-({[(5,6-dihydroxy-2- thien-2-ylpyrimidin-4- yl)carbonyl]amino}methyl)benzylca rbamate	457	A
	, C. C. C. C. C. C. C. C. C. C. C. C. C.			
131	**************************************	tert-butyl [3-({[(5,6-dihydroxy-2- thien-2-ylpyrimidin-4- yl)carbonyl]amino}	442	A
	no dia	methyl)phenyl]acetate	· .	
132		5,6-dihydroxy-N-[2-(1H-indol-3- yl)benzyl]-2-thien-2-ylpyrimidine-4- carboxamide	443	A
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133	S T N N N N N N N N N N N N N N N N N N	N-[3-(aminomethyl)benzyl]-5,6-dihydroxy-2-thien-2-ylpyrimidine-4-carboxamide (TFA salt)	357	A
134	S N N N N N N N N N N N N N N N N N N N	N-[2-(aminomethyl)benzyl]-5,6-dihydroxy-2-thien-2-ylpyrimidine-4 carboxamide	357	A
135		5,6-dihydroxy-N-[2-(1H-indol-3- ylmethyl)benzyl]-2-thien-2- ylpyrimidine-4-carboxamide	457	A .
136		tert-butyl 3-[2-({[(5,6-dihydroxy-2-thien-2-ylpyrimidin-4-yl)carbonyl]amino}methyl)benzyl]-1H-indole-1-carboxylate	1	A
137	HC OI	5,6-dihydroxy-N-[3-(1H-indol-3-ylmethyl)benzyl]-2-thien-2-ylpyrimidine-4-carboxamide	457	A

138	OH OH OH	tert-butyl 3-[3-({[(5,6-dihydroxy-2-thien-2-ylpyrimidin-4-yl)carbonyl]amino}methyl)benzyl]-1H-indole-1-carboxylate	557	A .
139		5,6-dihydroxy-N-[4-(1H-indol-3-ylmethyl)benzyl]-2-thien-2-ylpyrimidine-4-carboxamide	457	A
140		5,6-dihydroxy-N-[3-(1H-indol-3-yl)benzyl]-2-thien-2-ylpyrimidine-4-carboxamide	443	A
141		2-[3-({[(2-chlorobenzyl)amino]carbonyl}amino)thien-2-yl]-5,6-dihydroxypyrimidine-4-carboxamide	420	A
142		N-(2-chlorobenzyl)-2-[3-({[(2-chlorobenzyl)amino]carbonyl}amino)thien-2-yl]-5,6-dihydroxypyrimidine-4-carboxamide	42(M-1	A
143		5,6-dihydroxy-N-methyl-N-(1- naphthylmethyl)-2-thien-2- ylpyrimidine-4-carboxamide	392	A
14	4 Chiral Chiral	5,6-dihydroxy-N-[(1R)-1-(1- naphthyl)ethyl]-2-thien-2- ylpyrimidine-4-carboxamide	392	A

145					·
146	110	OH CHI	5.6-dihydroxy-N-[(1S)-1-(1-	392	A
146	145	J. OH	naphthyl)ethyl]-2-thien-2-	ł	- 1
146		, N J 0	Marginiding 4-carboxamide	1	
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147		N OH	· ·]	
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147	- 1			ļ	. 1
147	1	<u> </u>			
147	146	OH CHIM	5,6-dihydroxy-N-[(1R)-2-hydroxy-1-	358	A
4-carboxamide 5,6-dihydroxy-N-[2-(2-methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(4-nitrophenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide	170	<u> </u>	phenylethyl]-2-thien-2-ylpyrimidine-	· .	
147	- 1		4-carboxamide		
methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(4-nitrophenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dam-dam-dam-dam-dam-dam-dam-dam-dam-dam	1			.	
methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(4-nitrophenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide	1				•
methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(4-nitrophenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide	- 1				
methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(4-nitrophenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dam-dam-dam-dam-dam-dam-dam-dam-dam-dam					
methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(4-nitrophenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide			5 6 11 days N 12 (2	372	Δ
ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(4-nitrophenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide	147	р н	5,6-dihydroxy-N-[2-(2-	-3/2	Λ.
148	l	ii. OH	methoxyphenyl)ethyl]-2-thien-2-		
149 OH OH OH OH OH OH OH OH OH O	. 1		ylpyrimidine-4-carboxamide		
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ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(1H-indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-tindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-tindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-tindol-3-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[18-1-(4-tindol-3-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[18-1-(4-tindol-3-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide	148				
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yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R)-1-(4-methoxyphenyl)ethyl]-2-thien-2-	,		угругинише-4-сагроханиче		
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yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-dindol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R)-1-(4-methoxyphenyl)ethyl]-2-thien-2-			5 6 dibudeovy N. (2-(1H-indol-3-	381	A
carboxamide 5,6-dihydroxy-N-[2-(5-methoxy-1H-d11 indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R)-1-(4-methoxyphenyl)ethyl]-2-thien-2-	149	ρι	5,6-minydioxy-14-[2-(111-indor-5-	501	
5,6-dihydroxy-N-[2-(5-methoxy-1H- 411 A indol-3-yl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2- oxopyrrolidin-1-yl)propyl]-2-thien-2 ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R)-1-(4- arboxamide)] 5,6-dihydroxy-N-[(1R)-1-(4- arboxamide)] 5,6-dihydroxy-N-[(1R)-1-(4- arboxamide)]		N OH	yi)ethyij-2-tnien-2-yipyrimidine-4-		
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ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[3-(2-oxopyrrolidin-1-yl)propyl]-2-thien-2 ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R)-1-(4-methoxyphenyl)ethyl]-2-thien-2-	150	" " "	indol-3-vl)ethyll-2-thien-2-		1
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oxopyrrolidin-1-yl)propyl]-2-thien-2 ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R)-1-(4-methoxyphenyl)ethyl]-2-thien-2-	151	рн ·	5,6-dihydroxy-N-[3-(2-		A
ylpyrimidine-4-carboxamide ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R)-1-(4- 372 A methoxyphenyl)ethyl]-2-thien-2-	***	1 A	oxopyrrolidin-1-yl)propyl]-2-thien-2	l .	ļ
152 OH ONE SHEET S,6-dihydroxy-N-[(1R)-1-(4- 372 A methoxyphenyl)ethyl]-2-thien-2-	1	I . LLund	vlpyrimidine-4-carboxamide	l	[
methoxyphenyl)ethyl]-2-thien-2-	ļ.	I (T , I , ,)		Į	1
methoxyphenyl)ethyl]-2-thien-2-	1		1		1
methoxyphenyl)ethyl]-2-thien-2-		·	E C Jihudaan N ((1D) 1 (A	372	A
methoxyphenyl)ethyl]-2-tnien-2- ylpyrimidine-4-carboxamide	152		15,0-dinydroxy-14-[(1x)-1-(4-	""	
ylpyrimidine-4-carboxamide		, il Aut	methoxyphenyijethyij-2-tnien-2-		1
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153	OH OH	N-(1,3-benzodioxol-4-ylmethyl)-5,6- dihydroxy-2-thien-2-ylpyrimidine-4- carboxamide	372	A
154	S N N N N	N-(2-benzylphenyl)-5,6-dihydroxy- 2-thien-2-ylpyrimidine-4- carboxamide	404	A
155	J-1-00	N-(4-benzylphenyl)-5,6-dihydroxy- 2-thien-2-ylpyrimidine-4- carboxamide	404	A
156		N-(2,3-dihydro-1,4-benzodioxin-2- ylmethyl)-5,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide	386	A
157	ST CH	5,6-dihydroxy-N-[(1-pyrimidin-2-ylpiperidin-3-yl)methyl]-2-thien-2-ylpyrimidine-4-carboxamide (TFA salt)	413	A
158		5,6-dihydroxy-N-[(4- phenylmorpholin-2-yl)methyl]-2- thien-2-ylpyrimidine-4-carboxamide (TFA salt)	413	A
159	OH OH	5,6-dihydroxy-N-(2- phenylcyclopropyl)-2-thien-2- ylpyrimidine-4-carboxamide	354	

160 St. Chiral St. G-dihydroxy-N-[2-(2-phenyl-1H-indol-3-ylpethyl]-2-thien-2-ylpyrimidine-4-carboxamide Asylpyrimidine-4-carboxamide Asylpyrimidi			·		-
161	160	он		457	A
161 OH Chiral S,6-dihydroxy-2-thien-2- ylpyrimidine-4-carboxamide 162 OH Chiral S,6-dihydroxy-N-[(1R)-1-(3-methoxyphenyl)ethyl]-2-thien-2- ylpyrimidine-4-carboxamide 163 OH Chiral S,6-dihydroxy-N-[(1S)-1-(3-methoxyphenyl)ethyl]-2-thien-2- ylpyrimidine-4-carboxamide 164 OH Chiral S,6-dihydroxy-N-[(1S)-1-(3-methoxyphenyl)ethyl]-2-thien-2- ylpyrimidine-4-carboxamide 165 OH Chiral S,6-dihydroxy-N-[(1S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine 4-carboxamide 165 OH Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine 4-carboxamide 166 OH Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 167 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 168 OH Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 169 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 OH S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 OH S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 OH S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 OH S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 OH S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide		OH OH			
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162 OH Chiral 163 OH Chiral OH Chiral OH Chiral OH Chiral OH Chiral S,6-dihydroxy-N-[(1R)-1-(3-methoxyphenyl)-2-thien-2-ylpyrimidine-4-carboxamide 164 OH Chiral S,6-dihydroxy-N-[(1S)-1-(3-methoxyphenyl)-2-thien-2-ylpyrimidine-4-carboxamide 165 OH Chiral S,6-dihydroxy-N-[(1S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 166 OH Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 166 OH Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-phydroxy-1-ylpyrimidine-4-carboxamide 166 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 167 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 168 A S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 169 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 160 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide	101	ОН			
methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1S)-1-(3-methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 164 OH Chiral 5,6-dihydroxy-N-[(1S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-yhpenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 165 OH Chiral 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-yhpenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 166 Chiral 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-yhpenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 167 Chiral 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-yhpenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide		s LL N	ylpyrimidine-4-carboxamide		
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methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 163 Chiral S,6-dihydroxy-N-[(1S)-1-(3-methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 164 OH Chiral S,6-dihydroxy-N-[(1S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 165 OH Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-yhdroxy-1-yhdroxy-1-yhdroxy-1-yhdroxy-1-yhdroxy-1-yhdroxy-2-3-dihydroxy-N-[(1R,2S)-2-hydroxy-1-yhdroxy	162	QH Chiral	5,6-dihydroxy-N-[(1R)-1-(3-	372	Α.
163 OH Chiral S,6-dihydroxy-N-[(1S)-1-(3-methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 164 OH Chiral S,6-dihydroxy-N-[(1S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 165 OH Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 166 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 166 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 166 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 166 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 166 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 167 Chiral S,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 168 A A A A A A A A A A A A A		W C			
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methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 164 OH Chiral 5,6-dihydroxy-N-[(1S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 165 OH Chiral 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-yhdroxy-2,3-dihydro-1H-inden-1-yl] 2-thien-2-ylpyrimidine-4-carboxamide 166 ot tert-butyl 2-({2-[4-(aminocarbonyl)-5,6-dihydroxypyrimidin-2-yl]thien-3yl}amino)-2-oxo-1-]				
methoxyphenyl)ethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-ylpyrimidine-4-carboxamide 166 or tert-butyl 2-({2-[4-(aminocarbonyl)-5,6-dihydroxypyrimidin-2-yl]thien-3yl}amino)-2-oxo-1-	163	ÇH Chiral	5,6-dihydroxy-N-[(1S)-1-(3-	372	A
164 OH Chiral 5,6-dihydroxy-N-[(1S)-2-hydroxy-1-358 A phenylethyl]-2-thien-2-ylpyrimidine-4-carboxamide 165 OH Chiral 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-1-370 A hydroxy-2,3-dihydro-1H-inden-1-yl] 2-thien-2-ylpyrimidine-4-carboxamide 166 ot tert-butyl 2-({2-[4-(aminocarbonyl)-5,6-dihydroxypyrimidin-2-yl]thien-3yl}amino)-2-oxo-1-		,		.	
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4-carboxamide 4-carboxamide 5,6-dihydroxy-N-[(1R,2S)-2-hydroxy-N-[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl] 2-thien-2-ylpyrimidine-4-carboxamide 166 6t tert-butyl 2-({2-[4-(aminocarbonyl)-5,6-dihydroxypyrimidin-2-yl]thien-3yl}amino)-2-oxo-1-	164			358	A
OH Chiral 5,6-dihydroxy-N-[(1R,2S)-2- hydroxy-2,3-dihydro-1H-inden-1-yl] 2-thien-2-ylpyrimidine-4- carboxamide 166 ot tert-butyl 2-({2-[4-(aminocarbonyl)- 5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-		N OH	1 1		
hydroxy-2,3-dihydro-1H-inden-1-yl] 2-thien-2-ylpyrimidine-4- carboxamide tert-butyl 2-({2-[4-(aminocarbonyl)- 5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-		s	4-carboxamide		
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hydroxy-2,3-dihydro-1H-inden-1-yl] 2-thien-2-ylpyrimidine-4- carboxamide tert-butyl 2-({2-[4-(aminocarbonyl)- 5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-					
hydroxy-2,3-dihydro-1H-inden-1-yl] 2-thien-2-ylpyrimidine-4- carboxamide tert-butyl 2-({2-[4-(aminocarbonyl)- 5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-	165	OH Chimi	5,6-dihydroxy-N-[(1R,2S)-2-	370	A
carboxamide carboxamide tert-butyl 2-({2-[4-(aminocarbonyl)- 5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-	~~	ОН ОПИВИ		.]	
tert-butyl 2-({2-[4-(aminocarbonyl)- 5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-	.		2-thien-2-ylpyrimidine-4-	ĺ	
5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-]		carboxamide	1	*
5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-		но			
5,6-dihydroxypyrimidin-2-yl]thien-3 yl}amino)-2-oxo-1-					
yl}amino)-2-oxo-1-	166	OH		486	A
		N TON		.]	
pnenylethylcarbamate				1	
J. J. off or			pnenylethylcarbamate		
() ° 46		The star] .]		
		O° 46			
			<u> </u>	1	 ·

167	N 2-1	(3- amino(phenyl)acetyl]amino}thien- yl)-5,6-dihydroxypyrimidine-4- rboxamide (TFA salt)	386	A
168	CH CE	-(3- [amino(phenyl)acetyl]amino}thien- -yl)-N-benzyl-5,6- ihydroxypyrimidine-4- arboxamide (TFA salt)	476	A

Table	2		504	
1	OH A	N-(3-chlorobenzyl)-2-{4-[({[(2-chlorophenyl)sulfonyl]amino}carbo nyl)amino]thien-3-yl}-5,6- dihydroxypyrimidine-4- carboxamide	594	G
2	OH OH	N-benzyl-5,6-dihydroxy-2-thien-3- ylpyrimidine-4-carboxamide	328	A
3	OH OH OH,	2-[4-({[(2,3-dichlorobenzyl)amino]carbonyl} amino)thien-3-yl]-5,6-dihydroxy-N-methylpyrimidine-4-carboxamide	468	G

			(20	G
4		2-{4-[({[(2- chlorophenyl)sulfonyl]amino} carbonyl)amino]thien-3-yl}-N-(2,3- dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	620	G
5		N-benzyl-2-(4- {[(benzylamino)carbonyl]amino}-3- thienyl)-5,6-dihydroxy-4- pyrimidinecarboxamide	476	G
6		2-{4-[({[(2- chlorophenyl)sulfonyl]amino}carbo nyl)amino]thien-3-yl}-5,6- dihydroxy-N-(2- phenylethyl)pyrimidine-4- carboxamide	574	G ·
	OH OH OH,	2-{4-[({[(2- chlorophenyl)sulfonyl]amino} carbonyl)amino]thien-3-yl}-5,6- dihydroxy-N-methylpyrimidine-4- carboxamide	484	G
		N-benzyl-5,6-dihydroxy-2-[4- ({[(thien-2- ylmethyl)amino]carbonyl}amino)thi en-3-yl]pyrimidine-4-carboxamide	482	G

	9 0H N CH ₃	5,6-dihydroxy-N-methyl-2-[4- ({[(phenylsulfonyl)amino]carbonyl} amino)thien-3-yl]pyrimidine-4- carboxamide	450	G
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Table :	3		T	
1	OH OH F	N-(3,4-difluorobenzyl)-5,6- dihydroxy-2-(1,3-thiazol-2- yl)pyrimidine-4-carboxamide	365	A
2	S N OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (1,3-thiazol-2-yl)pyrimidine-4- carboxamide	347	A
3	SHAP OH CI	N-(3,4-dichlorobenzyl)-5,6- dihydroxy-2-(1,3-thiazol-2- yl)pyrimidine-4-carboxamide	397	A
4	OH OH OH	N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-(1,3-thiazol-2-yl)pyrimidine-4- carboxamide	373	A
5	OH OH N N N N N N N N N N N N N N N N N	N-(3-fluorobenzyl)-5,6-dihydroxy-2 (1,3-thiazol-2-yl)pyrimidine-4- carboxamide	347	A

6	OH	N-(2,4-difluorobenzyl)-5,6-	365	A
1	↓ ,oH	dihydroxy-2-(1,3-thiazol-2-	- 1	
- 1	N	yl)pyrimidine-4-carboxamide		•
1	s N			
1			1	
- 1			.	
	•			
7	ÓН	5,6-dihydroxy-N-(1-	379	A
1	↓ OH	naphthylmethyl)-2-(1,3-thiazol-2-	į	
- 1		yl)pyrimidine-4-carboxamide	. [
1	S N		1	
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	·	0.56.11.1.0	262	
8	он	N-(2-chlorobenzyl)-5,6-dihydroxy-2	363	A
- 1	N OH	(1,3-thiazol-2-yl)pyrimidine-4-	1	
- 1		carboxamide	Ì	
	SYN			
	UN Ö Ä			
	•	·		
		5,6-dihydroxy-N-(2-methoxybenzyl)	359	A
9	OH L au	2-(1,3-thiazol-2-yl)pyrimidine-4-	337	•
	N OH	carboxamide		
	s N	carooxamide		
H	1		1	
1	CH ₃			
		;		
		N-(4-chlorobenzyl)-5,6-dihydroxy-2	363	A
10	OH A	(1,3-thiazol-2-yl)pyrimidine-4-		
	N OH OH	carboxamide		
1	s N			
1				-
1	EN O		· ·	
	•			
11	OH	N-(3-chloro-2-methylbenzyl)-5,6-	377	A
**	OH	dihydroxy-2-(1,3-thiazol-2-	[
		yl)pyrimidine-4-carboxamide		
,	s N N C			ı .
	UN 6 CH,		1	1
·			· ·	1
			 	
12	Ģн F	N-(2,5-difluorobenzyl)-5,6-	365	A
	JOH J	dihydroxy-2-(1,3-thiazol-2-	Ī	
		yl)pyrimidine-4-carboxamide	}	
	s N			1
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1		<u> </u>	1	L

		T. (19 2	415	A]
13	N OH F	N-[4-fluoro-3- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-(1,3-thiazol-2- yl)pyrimidine-4-carboxamide	413	A
14	OH FFF	N-[3-fluoro-5- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-(1,3-thiazol-2- yl)pyrimidine-4-carboxamide	415	A
15	OH OH OH, OH,	N-(3,4-dimethoxybenzyl)-5,6- dihydroxy-2-(1,3-thiazol-2- yl)pyrimidine-4-carboxamide	389	A
16	S N OH S F F	5,6-dihydroxy-2-(1,3-thiazol-2-yl)- N-[2- (trifluoromethyl)benzyl]pyrimidine- 4-carboxamide	397	A
17	OH F N OH F	N-(3,5-difluorobenzyl)-5,6- dihydroxy-2-(1,3-thiazol-2- yl)pyrimidine-4-carboxamide	365	A
18	SH OH OH	5,6-dihydroxy-N-(3-methoxybenzyl) 2-(1,3-thiazol-2-yl)pyrimidine-4- carboxamide	359	A
19	OH OH CH3	N-(3,4-dimethylbenzyl)-5,6-dihydroxy-2-(1,3-thiazol-2-yl)pyrimidine-4-carboxamide	357	A

20	ÓН	N-benzyl-5,6-dihydroxy-2-(1,3-	329	A
	OH	thiazol-2-yl)pyrimidine-4-		
		carboxamide	•	
	s N			
21	ÓН	N-(1-benzothien-3-ylmethyl)-5,6-	385	A.
	OH S	dihydroxy-2-(1,3-thiazol-2-	•	
		yl)pyrimidine-4-carboxamide		
'	S N N	· .		
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	· · · · · · · · · · · · · · · · · · ·			
22	ÓН	N-(2,3-dihydro-1H-inden-1-yl)-5,6-	355	A
	OH	dihydroxy-2-(1,3-thiazol-2-		
		yl)pyrimidine-4-carboxamide		
	« The state of the	1 .	-	l .
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23	ОН	N-(2,3-dihydro-1H-inden-2-yl)-5,6-	355	A
	ОН	dihydroxy-2-(1,3-thiazol-2-		
		yl)pyrimidine-4-carboxamide		
.	(ST) N T			
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1 1				
24	он сң	5,6-dihydroxy-N-(4-methoxybenzyl)	359	A
	N OH O	2-(1,3-thiazol-2-yl)pyrimidine-4-		
		carboxamide		
	WN Ö	`		
			200	
25	он	N-(3-chloro-4-methylbenzyl)-5,6-	377	A
	N OH CH	dihydroxy-2-(1,3-thiazol-2-		•
		yl)pyrimidine-4-carboxamide	-	,
	N O			
			415	
26	OH _	N-[4-fluoro-2-	413	A
.	OH OF	(trifluoromethyl)benzyl]-5,6-		
		dihydroxy-2-(1,3-thiazol-2-		
	NOT NOT Y	yl)pyrimidine-4-carboxamide		
·	Win · ö F→r	'.		
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27	N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-(1,3-thiazol-2-yl)pyrimidine-4-carboxamide	389	A
28	N-(1,3-benzodioxol-5-ylmethyl)-5,6-dihydroxy-2-(1,3-thiazol-2-yl)pyrimidine-4-carboxamide	373	A
2.9	OH CH, 5,6-dihydroxy-2-(1,3-thiazol-2-yl)-N-(2,4,6-trimethoxybenzyl)pyrimidine-4-carboxamide	419	A
3	OH CH, N-(2,4-dimethoxybenzyl)-5,6-dihydroxy-2-(1,3-thiazol-2-yl)pyrimidine-4-carboxamide	389	A
	N-benzyl-5,6-dihydroxy-2-(6-methoxy-1,3-benzothiazol-2-yl)pyrimidine-4-carboxamide	409	A

Table 4	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (2-methyl-1,3-thiazol-4- yl)pyrimidine-4-carboxamide	361	A
2 H,C-N-N-N-F	N-(2,4-difluorobenzyl)-5,6- dihydroxy-2-(2-methyl-1,3-thiazol-4 yl)pyrimidine-4-carboxamide	379	A

3	H _C C-NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	N-benzyl-5,6-dihydroxy-2-(2- methyl-1,3-thiazol-4-yl)pyrimidine- 4-carboxamide	343	A
4	JOH NO.	N-(1,3-benzodioxol-5-ylmethyl)-5,6- dihydroxy-2-(2-methyl-1,3-thiazol-4 yl)pyrimidine-4-carboxamide	387	A
5	OH	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(2-methyl-1,3-thiazol-4 yl)pyrimidine-4-carboxamide	403	A

Table 5	·	T	
OH OH	N-benzyl-5,6-dihydroxy-2-(2- methylphenyl)pyrimidine-4- carboxamide	336	A
] a N	N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-(2-methylphenyl)pyrimidine-4- carboxamide	380	A
3 OH OH FF	N-[4-fluoro-3- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-(2- methylphenyl)pyrimidine-4- carboxamide	422	A
4 OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (2-methylphenyl)pyrimidine-4- carboxamide	354	A

5	CH, N CH, CH, CH,	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(2- methylphenyl)pyrimidine-4- carboxamide	396	A
6	CH, N OH CH,	N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2-(2- methylphenyl)pyrimidine-4- carboxamide	384	A
7	CH, N CH OH, OH,	5,6-dihydroxy-N-(3-methoxybenzyl) 2-(2-methylphenyl)pyrimidine-4- carboxamide	366	A
8	CH ₃ N OH F	N-(3,4-difluorobenzyl)-5,6- dihydroxy-2-(2- methylphenyl)pyrimidine-4- carboxamide	372	A
9	CH, NOH OH	N-(2,4-difluorobenzyl)-5,6- dihydroxy-2-(2- methylphenyl)pyrimidine-4- carboxamide	372	A
10	OH OH	N-benzyl-5,6-dihydroxy-2- phenylpyrimidine-4-carboxamide	322	A
11		N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-{2-[(pyridin-2-ylcarbonyl)amino]phenyl}pyrimidin e-4-carboxamide	502	I
12	CH ₃ N OH F	N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-(2- methylphenyl)pyrimidine-4- carboxamide	422	A

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13	OH OH	N-(2,3-dihydro-1H-inden-2-yl)-5,6- dihydroxy-2-phenylpyrimidine-4-	348	A
	N Y	carboxamide		
	N N	Carboxamide	1	
		[
			1	
14	ОН	N-(2,3-dimethoxybenzyl)-5,6-	382	A
14			302	A
	N OH	dihydroxy-2-phenylpyrimidine-4-	. 1	
1		carboxamide		-
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15	ОН	N-(2,3-dimethoxybenzyl)-5,6-	502	I
	in ✓ OH ✓	dihydroxy-2-[2-	į	
		(isonicotinoylamino)	j	
		phenyl]pyrimidine-4-carboxamide		
	``N ``OL		. [
		(HCL salt)		
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		N-benzyl-2-[2-({[(2,3-	538	G
16	I au		ا ەدد	J
		dichlorobenzyl)amino]carbonyl}ami	Į.	
.		no)phenyl]-5,6-	ļ	
	🌭 ,	dihydroxypyrimidine-4-		
		carboxamide	.]	
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		1 -14 (((2) (4)	582	
17	م س ا	benzyl 4-{[(2-{4-	202	Ţ
	المللما	[(benzylamino)carbonyl]-5,6-		
	\ \\ \." \\	dihydroxypyrimidin-2-	- 1	
		yl}phenyl)amino]carbonyl}piperidi	- 1	
	ا ت للم	ne-1-carboxylate	.]	
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18	QH .	N-benzyl-5,6-dihydroxy-2-[2-(1-	478	A
.	, de .	naphthylmethoxy)phenyl]pyrimidin		
.		e-4-carboxamide	l	
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		N. 1 1 2 (2 (11/2 5	· 538	G
19	он , , , , , , , , , , , , , , , , , , ,	N-benzyl-2-[2-({[(2,5-	، عدد	G
		dichlorobenzyl)amino]carbonyl}ami		
l		no)phenyl]-5,6-	. [
1	🍑 . °	dihydroxypyrimidine-4-		
l	م بہ ا	carboxamide	}	-
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20	CH Co. CH,	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-{2-[(pyridin-3- ylcarbonyl)amino]phenyl}pyrimidin e-4-carboxamide (TFA salt)	502	I
21		N-{2-[4-(aminocarbonyl)-5,6- dihydroxypyrimidin-2- yl]phenyl}phenylalaninamide (TFA salt)	394	A*
22		tert-butyl 3-({3-[4-(aminocarbonyl)-5,6-dihydroxypyrimidin-2-yl]phenyl}amino)-3-oxo-1-phenylprop-2-ylcarbamate	494.2	I

Table 6	N-(3-chloro-4-fluorobenzyl)-5,6- dihydroxy-2-(3- methylphenyl)pyrimidine-4- carboxamide	388	A
2 OH OH OH OH,	N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2-(3- methylphenyl)pyrimidine-4- carboxamide	384	A
3	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [3-(morpholin-4- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	439	В
4 HC HC N OH	N-(3-chlorobenzyl)-5,6-dihydroxy-2 (3-methylphenyl)pyrimidine-4- carboxamide	370	A

	•	•		
5	OH OH OF	2-{3-[(diethylamino)methyl]phenyl} N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-	425	В
. :	You.	carboxamide (TFA salt)		
	Ol,			
6		N-benzyl-5,6-dihydroxy-2-(3- nitrophenyl)pyrimidine-4- carboxamide	367	A
7		N-(3-chloro-4-methylbenzyl)-2-{3- [(diethylamino)methyl]phenyl}-5,6- dihydroxypyrimidine-4-	455	В
		carboxamide (HCl salt)	· .	
8	on Car	N-(3-chloro-4-methylbenzyl)-2-{3- [(diisopropylamino)methyl]phenyl}-	483	В
		5,6-dihydroxypyrimidine-4- carboxamide (HCl salt)		
	HC CH			
9	OH OH	N-benzyl-5,6-dihydroxy-2-(3-methylphenyl)pyrimidine-4-carboxamide	336	A
•				
10	OH OH	N-(1,1'-biphenyl-3-ylmethyl)-5,6- dihydroxy-2-(3- methylphenyl)pyrimidine-4-	412	A
		carboxamide		
11	N CH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {3-[(2-oxopyridin-1(2H)-	447	A
		yl)methyl]phenyl}pyrimidine-4- carboxamide		
	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\		255	
12	H _C C JH OH	5,6-dihydroxy-N-(2-methoxybenzyl) 2-(3-methylphenyl)pyrimidine-4- carboxamide	366	A
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			405	- D
13		N-benzyl-5,6-dihydroxy-2-[3- (pyrrolidin-1- ylmethyl)phenyl]pyrimidine-4- carboxamide (HCl salt)	405	В
14	CH, CH, CH, CH, CH, CH, CH, CH, CH, CH,	2-{3- [(dimethylamino)methyl]phenyl}-N- (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	397	В
15		N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2-{3-[(2-oxopyridin- 1(2H)-yl)methyl]phenyl}pyrimidine- 4-carboxamide	477	A
16		N-(3,4-difluorobenzyl)-5,6- dihydroxy-2-{3-[(2-oxopyridin- 1(2H)-yl)methyl]phenyl}pyrimidine- 4-carboxamide	465	A
17		N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-{3-[(2-oxopyridin- 1(2H)-yl)methyl]phenyl}pyrimidine- 4-carboxamide	515	A
18	H,C OH OH OH, OH,	N-(2,3-dimethylbenzyl)-5,6-dihydroxy-2-(3-methylphenyl)pyrimidine-4-carboxamide	364	A
19	OH OH	2-(3-bromophenyl)-N-(2,3-dihydro- 1H-inden-2-yl)-5,6- dihydroxypyrimidine-4- carboxamide	426	A
20	Change Control of the	N-(4-fluorobenzyl)-5,6-dihydroxy-2 {3-[(4-methylpiperazin-1- yl)methyl]phenyl}pyrimidine-4- carboxamide (TFA salt)	452	В

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21		I-(4-fluorobenzyl)-5,6-dihydroxy-2- 3-(piperidin-1- lmethyl)phenyl]pyrimidine-4- arboxamide (TFA salt)	437	В
22	d 1	V-(1,3-benzodioxol-5-ylmethyl)-5,6- lihydroxy-2-{3-{(2-oxopyridin- (2H)-yl)methyl]phenyl}pyrimidine -carboxamide	473	A
23		N-(3-chloro-4-methylbenzyl)-2-{3- (3,5-dimethylpiperazin-1- /l)methyl]phenyl}-5,6- lihydroxypyrimidine-4- carboxamide (TFA salt)	496	В
24		N-benzyl-5,6-dihydroxy-2-{3-[(2- oxopyridin-1(2H)- yl)methyl]phenyl}pyrimidine-4- carboxamide	429	A
25		N-(2,4-dimethoxybenzyl)-5,6- dihydroxy-2-{3-[(2-oxopyridin- 1(2H)-yl)methyl]phenyl}pyrimidine- 4-carboxamide	489	A
26		N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[3-(pyrrolidin-1-ylmethyl)phenyl]pyrimidine-4-carboxamide (TFA salt)	465	В
27	AC NC COL	2-{3- [(diisopropylamino)methyl]phenyl}- N-(2,3-dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	495	В
28		5,6-dihydroxy-N-(3-methoxybenzyl 2-{3-[(2-oxopyridin-1(2H)- yl)methyl]phenyl}pyrimidine-4- carboxamide	459	A

				
29	H,C CH, CH, CH, CH, CH, CH, CH, CH, CH,	N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-(3-methylphenyl)pyrimidine-4-carboxamide	396	A .
30		N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-{3-[(2-oxopyridin-1(2H)-yl)methyl]phenyl}pyrimidine-4-carboxamide	489	A
31	### C	5,6-dihydroxy-2-(3-methylphenyl)- N-(3-phenylprop-2-ynyl)pyrimidine- 4-carboxamide	360	A
32	HCN CH	N-benzyl-2-{3- [(dimethylamino)methyl]phenyl}- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	379	В
33		N-benzyl-2-[3-({[(3,4-dichlorobenzyl)amino]carbonyl}amino)phenyl]-5,6-dihydroxypyrimidine-4-carboxamide	539	G
34		N-benzyl-5,6-dihydroxy-2-[3- (piperidin-1- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	419	В
35	CH OH COH	N-benzyl-2-{3-[(3,5-dimethylpiperazin-1-yl)methyl]phenyl}-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)	448	В
36	MC COL	2-{3- [(dimethylamino)methyl]phenyl}-N- [3-fluoro-4-(trifluoromethyl)benzyl} 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	465	В

		5 (479	В
37	он	N-(2,3-dimethoxybenzyl)-5,6-	4/9	В
1	N CON	dihydroxy-2-[3-(piperidin-1-	1	
		ylmethyl)phenyl]pyrimidine-4-		
- 4		carboxamide (TFA salt)	. 1	- 1
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	<i>Y</i>)			
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38	CH	N-(2,3-dimethoxybenzyl)-2-{3-	439	В.
	ОН	[(dimethylamino)methyl]phenyl}-		
		5,6-dihydroxypyrimidine-4-		
		carboxamide (TFA salt)		
	Ha. J			
	, de			
			467	В
39	ф	2-{3-[(diethylamino)methyl]phenyl}	40/	D .
	NA CON	N-(2,3-dimethoxybenzyl)-5,6-	1	
	A NOON	dihydroxypyrimidine-4-		
	الما الما	carboxamide (TFA salt)	1	
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		2. (2. 2)	607	В
40	он .	N-(2,3-dimethoxybenzyl)-5,6-	''''	
		dihydroxy-2-(3-{[(2,4,5-		
		trichlorophenyl)thio]methyl}phenyl)		İ
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· ·	à	·		
41	CH CH	5,6-dihydroxy-2-(3-nitrophenyl)-N-	315	A
**	J OH	prop-2-ynylpyrimidine-4-		
1		carboxamide	1	
	l 🜱 °			
1	0-160			
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Tabl	e 7	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (4-methylphenyl)pyrimidine-4- carboxamide	354	A
2	CH CH CH	N-(2,4-difluorobenzyl)-5,6- dihydroxy-2-(4- methylphenyl)pyrimidine-4- carboxamide	372	A

3	H,C OH OH N F F	5,6-dihydroxy-2-(4-methylphenyl)- N-[2- (trifluoromethyl)benzyl]pyrimidine- 4-carboxamide	404	A
4	HC OH OH FF	N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-(4- methylphenyl)pyrimidine-4- carboxamide	422	A
5	H ₃ C OH OH OH	N-(4-chlorobenzyl)-5,6-dihydroxy-2 (4-methylphenyl)pyrimidine-4- carboxamide	370	A
	HC OH OH	N-(1,3-benzodioxol-5-ylmethyl)-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide	380	A
		N-(3-chloro-4-methylbenzyl)-5,6-dihydroxy-2-[4-(pyrrolidin-1-ylmethyl)phenyl]pyrimidine-4-carboxamide (TFA salt)	453	В
		N-(4-fluorobenzyl)-5,6-dihydroxy-2 [4-(pyrrolidin-1- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	423	В
		N-(3,4-dimethylbenzyl)-5,6-dihydroxy-2-[4-(morpholin-4-ylmethyl)phenyl]pyrimidine-4-carboxamide (TFA salt)	449	В
		N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-[4-(morpholin-4- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	465	В

11	안	N-(3-chloro-4-methylbenzyl)-5,6-	469	В
- 1	" o"	dihydroxy-2-[4-(morpholin-4-	1	
- 1		ylmethyl)phenyl]pyrimidine-4-	ļ	. 1
1	~~~ \\	carboxamide (TFA salt)		
.			1	
1		1		
		27 (4 Cl - 1 1) 5 6 dibudency 2	439	В
12	OH _OH ·	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	737	
1		[4-(morpholin-4-	1	
		ylmethyl)phenyl]pyrimidine-4-		
		carboxamide (TFA salt)		
.]	V			
- 1	· •	·	. [
12		N-(3-chlorobenzyl)-5,6-dihydroxy-2	370	A
13	OH OH	(4-methylphenyl)pyrimidine-4-		ļ
		carboxamide		
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	nc " "			
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			-070	
14	ÓН	N-(3,4-difluorobenzyl)-5,6-	372	A
٠	J, OH , ✓ F	dihydroxy-2-(4-		
		methylphenyl)pyrimidine-4-	1	
İ	F C	carboxamide	· 1	
	H _C C "			
		1	· 1	
		2-{4-	407	В
15	,	[(dimethylamino)methyl]phenyl}-N-		
		(3,4-dimethylbenzyl)-5,6-		
		dihydroxypyrimidine-4-	1	
		carboxamide (TFA salt)		
	H ₂ C	Carobxanide (1171 said)		
	οι,	<u> </u>		
16	۴ ۔.	N-(3-chloro-4-methylbenzyl)-2-{4-	427	В
		[(dimethylamino)methyl]phenyl}-		
		5,6-dihydroxypyrimidine-4-		
1	\ \ \	carboxamide (TFA salt)		
[· ·		
	į č4,	•		
		N-(3-chloro-4-methylbenzyl)-2-{4-	455	В
17	<u></u>	[(diethylamino)methyl]phenyl}-5,6-	i .	
	I MC STATE		1	
	I make by	dihydroxypyrimidine-4-	1	
		carboxamide (TFA salt)	!	1
		1 '	1	1
	7		<u> </u>	L
18	ÇH	2-{4-[(diethylamino)methyl]phenyl}	425	В
10		N-(4-fluorobenzyl)-5,6-		
[I May properly to	dihydroxypyrimidine-4-	1	
1:	I HAVE TO THE TOTAL THE TO	carboxamide (TFA salt)	1	
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			467	В
19	OH 1 OH	N-(3-chloro-4-methylbenzyl)-5,6-	407	В
		dihydroxy-2-[4-(piperidin-1-	1	
-		ylmethyl)phenyl]pyrimidine-4-	1	
	~~~ ]	carboxamide (TFA salt)	1	
			- 1	
			- 1	
1				
20	QH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	437	В
20		[4-(piperidin-1-	j	
- 1		ylmethyl)phenyl]pyrimidine-4-		
- 1		carboxamide (TFA salt)	j	
- 1		carboxamide (114 sat)		
- 1		1	1	
	<u>,</u>	<u> 1</u>		
		N-(1,1'-biphenyl-3-ylmethyl)-5,6-	412	A
21	) on a	dihydroxy-2-(4-	- 1	
	Marie Contraction	methylphenyl)pyrimidine-4-	1	
- 1				
1		carboxamide		
	нс 🐣		1	
		N-(2,3-dimethoxybenzyl)-5,6-	481	В
22	он	dihydroxy-2-[4-(morpholin-4-	ļ	
1	y ar	diffydioxy-2-[4-(morphonia 4	1	
- 1		ylmethyl)phenyl]pyrimidine-4-	l	
	الملك المالك المالك المالك المالك المالك المالك المالك المالك المالك المالك المالك المالك المالك المالك المالك	carboxamide (TFA salt)	1	
1	<b>.</b> ,		- 1	
			- 1	•
		N-(2-ethoxybenzyl)-5,6-dihydroxy-	380	A
23	0H 	2-(4-methylphenyl)pyrimidine-4-	1	
	N CH	carboxamide	1	
ı		carboxamide		
1		i	1	
	н,с о		i i	
	. ભ્	]		
	. сң	N-14-fluoro-3-	422	
24	. оң	N-[4-fluoro-3-	422	A
24	OH OH	(trifluoromethyl)benzyl]-5,6-	422	A
24	OH OH F	(trifluoromethyl)benzyl]-5,6- dihydroxy-2-(4-	422	A
24	OH OH FF	(trifluoromethyl)benzyl]-5,6- dihydroxy-2-(4- methylphenyl)pyrimidine-4-	422	A
24	OH, OH OH FF	(trifluoromethyl)benzyl]-5,6- dihydroxy-2-(4-	422	A
24	OH OH OH	(trifluoromethyl)benzyl]-5,6- dihydroxy-2-(4- methylphenyl)pyrimidine-4-	422	A
	H,C OH OH FF	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide		A
24	H,C OH OH FF	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl)		-
	H,C OH OH FF	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-		-
	H,C OH OH FF	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl)		-
	OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-		-
	H,C OH OH FF	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-		-
	OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide	366	A
25	H,C OH OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide		-
	H,C OH OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide  N-(2-ethoxybenzyl)-5,6-dihydroxy-	366	A
25	H,C OH OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide  N-(2-ethoxybenzyl)-5,6-dihydroxy-2-{4-[(4-methylpiperazin-1-	366	A
25	H,C OH OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide  N-(2-ethoxybenzyl)-5,6-dihydroxy-2-{4-[(4-methylphenyl)pyrimidine-4-yl)methyl]phenyl}pyrimidine-4-	366	A
25	H,C OH OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide  N-(2-ethoxybenzyl)-5,6-dihydroxy-2-{4-[(4-methylpiperazin-1-	366	A
25	H,C OH OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide  N-(2-ethoxybenzyl)-5,6-dihydroxy-2-{4-[(4-methylphenyl)pyrimidine-4-yl)methyl]phenyl}pyrimidine-4-	366	A
25	H,C OH OH OH OH OH OH	(trifluoromethyl)benzyl]-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(3-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4-carboxamide  N-(2-ethoxybenzyl)-5,6-dihydroxy-2-{4-[(4-methylphenyl)pyrimidine-4-yl)methyl]phenyl}pyrimidine-4-	366	A

27		N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2-{4-[(4-methylpiperazin 1-yl)methyl]phenyl}pyrimidine-4- carboxamide (TFA salt)	482	В
	Ċų			
28		N-(4-fluorobenzyl)-5,6-dihydroxy-2- {4-[(4-methylpiperazin-1- yl)methyl]phenyl}pyrimidine-4- carboxamide (TFA salt)	452	В
29		N-(3,4-dimethylbenzyl)-5,6-dihydroxy-2-[4-(piperidin-1-ylmethyl)phenyl]pyrimidine-4-carboxamide (TFA salt)	447	В
30		N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-[4-(piperidin-1- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	463	В
31		N-(4-fluorobenzyl)-5,6-dihydroxy-2- [4-(1-morpholin-4- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	453	В
32		2-{4- [(dimethylamino)methyl]phenyl}-N- (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	397	В
33		2-{4-[(diethylamino)methyl]phenyl} N-(3,4-dimethylbenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	435	В
34	H ₂ C	2-{4-[(diethylamino)methyl]phenyl} N-(2-ethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	451	В
1		<u> </u>	1	

N COH,	dihydroxy-2-(4- methylphenyl)pyrimidine-4-	384	A
H,CC OH,	5,6-dihydroxy-N-(4-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4- carboxamide	366	A
HC NO CHOCK	N-(2,3-dimethoxybenzyl)-2-{4- [(dimethylamino)methyl]phenyl}- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	439	В
HE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CONTROL OF THE CON	N-(3,4-dimethylbenzyl)-5,6-dihydroxy-2-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}pyrimidine-4-carboxamide (TFA salt)	462	В
Ho Mary	2-{4- [(dimethylamino)methyl]phenyl}-N- (2-ethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	423	В
MC C C C C C C C C C C C C C C C C C C	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {4-[1-(4-methylpiperazin-1- yl)ethyl]phenyl}pyrimidine-4- carboxamide (TFA salt)	466	В
OH OH CH, CH,	N-(2,3-dimethylbenzyl)-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide	364	A
CH OH OH C	N-(2-chloro-4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide	388	A
	HC () () () () () () () () () () () () ()	Recommide  N-(2,3-dimethoxybenzyl)-2-{4- [(dimethylamino)methyl]phenyl}- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)  N-(3,4-dimethylbenzyl)-5,6- dihydroxy-2-{4-[(4-methylpiperazin-1- yl)methyl]phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- [4-[1-(4-methylpiperazin-1- yl)ethyl]phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethylbenzyl)-5,6-dihydroxy-2- [4-[1-(4-methylpiperazin-1- yl)ethyl]phenyl]pyrimidine-4- carboxamide  N-(2,3-dimethylbenzyl)-5,6- dihydroxy-2-(4- methylphenyl)pyrimidine-4- carboxamide  N-(2-chloro-4-fluorobenzyl)-5,6- dihydroxy-2-(4- methylphenyl)pyrimidine-4- carboxamide	dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide  5,6-dihydroxy-N-(4-methoxybenzyl) 366  2-(4-methylphenyl)pyrimidine-4-carboxamide  N-(2,3-dimethoxybenzyl)-2-(4-[(dimethylamino)methyl]phenyl]-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)  N-(3,4-dimethylbenzyl)-5,6-dihydroxy-2-(4-[(dimethylamino)methyl]phenyl]-N-(arboxamide (TFA salt)  2-(4-[(dimethylamino)methyl]phenyl]-N-(2-ethoxybenzyl)-5,6-dihydroxy-2-(4-methylpiperazin-1-yl)methylpyrimidine-4-carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-[(4-methylpiperazin-1-yl)ethyl]phenyl]pyrimidine-4-carboxamide (TFA salt)  N-(2,3-dimethylpenyl)pyrimidine-4-carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylpiperazin-1-yl)ethylphenyl]pyrimidine-4-carboxamide  N-(2,3-dimethylbenzyl)pyrimidine-4-carboxamide (TFA salt)  N-(2-chloro-4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide

OH OH	N-benzyl-5,6-dihydroxy-2-(4- methylphenyl)pyrimidine-4- carboxamide	336	A
Ho			
OH OH	5,6-dihydroxy-N-(2-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4- carboxamide	366	A
HC CH,			
~ (**)	N-(3,4-dimethylbenzyl)-5,6-dihydroxy-2-[4-(pyrrolidin-1-	433	В
	carboxamide (TFA salt)		·
	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [4-(1-piperidin-1- ylethyl)phenyl]pyrimidine-4-	451	В
<del>O</del>	carboxamide (1rA sait)		
MC CH COL	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-[4-(1-morpholin-4- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	495	В
Q	1000	500	
	N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-{4-[1-(4-methylpiperazin-1-yl)ethyl]phenyl}pyrimidine-4-carboxamide (TFA salt)	308	В
H,C OH OH OH OH OH OH OH OH	N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-(4-methylphenyl)pyrimidine-4-carboxamide	396	A
OH OH F	N-(3-chloro-4-fluorobenzyl)-5,6- dihydroxy-2-(4- methylphenyl)pyrimidine-4-	388	A
	H, CH N CH N CH N CH N CH N CH N CH N CH	methylphenyl)pyrimidine-4- carboxamide  5,6-dihydroxy-N-(2-methoxybenzyl) 2-(4-methylphenyl)pyrimidine-4- carboxamide  N-(3,4-dimethylbenzyl)-5,6- dihydroxy-2-[4-(pyrrolidin-1- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- [4-(1-piperidin-1- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-[4-(1-morpholin-4- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-[4-[1-(4- methylpiperazin-1- yl)ethyl]phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(4-[1-(4- methylpiperazin-1- yl)ethyl]phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(3,4-dimethylpenzyl)-5,6- dihydroxy-2-[4-(1-morpholin-4- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(3,4-dimethylpenzyl)-5,6- dihydroxy-2-(4-[1-(4- methylpiperazin-1- yl)ethyl]phenyl]pyrimidine-4- carboxamide (TFA salt)	methylphenyl)pyrimidine-4- carboxamide  5,6-dihydroxy-N-(2-methoxybenzyl) 366 2-(4-methylphenyl)pyrimidine-4- carboxamide  N-(3,4-dimethylbenzyl)-5,6- dihydroxy-2-[4-(pyrrolidin-1- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- [4-(1-piperidin-1- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-[4-(1-morpholin-4- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(4-[1-4-methylpiperzin-1- ylethyl]phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(4-methylpiperzin-1- ylethyl]phenyl]pyrimidine-4- carboxamide (TFA salt)  N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(4-methylpiperzin-1- ylethylphenyl)pyrimidine-4- carboxamide  N-(3,4-dimethylphenyl)pyrimidine-4- carboxamide (TFA salt)

PCT/GB02/04742

51	MC MC MC MC MC MC MC MC MC MC MC MC MC M	2-{4-[(diethylamino)methyl]phenyl} N-(2,3-dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	467	В
52		N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(piperidin-1-ylmethyl)phenyl]pyrimidine-4-carboxamide (TFA salt)	479	В
53		N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-[4-(pyrrolidin-1- ylmethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	449	В
54	HICK OH OH OH	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-[4-(1-piperidin-1- ylethyl)phenyl]pyrimidine-4- carboxamide (TFA salt)	493	В
55		N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}pyrimidine-4-carboxamide (TFA salt)	494	В
56		N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(pyrrolidin-1-ylmethyl)phenyl]pyrimidine-4-carboxamide (TFA salt)	465	В

Table 8	N-(3-chloro-4-methylbenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	292 (M-)	F
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2	OH OH F	N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	262 (M-)	F
3	OH N F F	N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6- dihydroxypyrimidine-4- carboxamide	332	F
4	OH N OCH,	N-(2,3-dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	304 (M-)	F
5	OH CH3	N-(3,4-dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	306	F

Table	. 9		2000	
1		N4-(4-fluorobenzyl)-5,6-dihydroxy- N2-(pyridin-2-ylmethyl)pyrimidine- 2,4-dicarboxamide (TFA salt)	396(M-)	H
2		N-(4-fluorobenzyl)-5,6-dihydroxy-2 (piperazin-1-ylcarbonyl)pyrimidine- 4-carboxamide (TFA salt)		Ħ
3		N4-(4-fluorobenzyl)-5,6-dihydroxy- N2-(2-morpholin-4- ylethyl)pyrimidine-2,4- dicarboxamide (TFA salt)	420	H

4	N OH	N,N'-dibenzyl-5,6- dihydroxypyrimidine-2,4- dicarboxamide	379	Н .
5.		N2-(4-fluorobenzyl)-5,6-dihydroxy- N4-(2-morpholin-4- ylethyl)pyrimidine-2,4- dicarboxamide (TFA salt)	420	H

Ta	ble 1	OH	2-benzyl-N-(2,4-difluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	372	A
	2	i i	2-(benzyloxycarbonylaminomethyl)- N-(2,4-difluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	445	A
	3	Chy N J H OH	N-[(4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2- yl)methyl]morpholine-4- carboxamide	406	G
	4	Clay NIT NIT	2-(benzyloxycarbonylaminomethyl)- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	427	A
	5		2-(benzyloxycarbonylaminomethyl)- N-(1-naphthylmethyl)-5,6- dihydroxypyrimidine-4- carboxamide	459	A
		•			

		•		
6	OH OH OH	2-benzyl-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	354	A
7	ОН	2-benzyl-5,6-dihydroxy-N-(1-naphthylmethyl)pyrimidine-4-	386	A
		carboxamide		
8	OH OH	2-benzyl-N-(3-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	354	A
9		2-benzyl-N-(3,4-difluorobenzyl)-5,6 dihydroxypyrimidine-4- carboxamide	372	A
	ö			·
10		2-(1,3-benzodioxol-5-ylmethyl)-N- (3,4-difluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	416	A
11		2-(1,3-benzodioxol-5-ylmethyl)-N- [4-fluoro-2-(trifluoromethyl)benzyl}- 5,6-dihydroxypyrimidine-4- carboxamide	466	A
12		N-(4-fluorobenzyl)-5,6-dihydroxy-2- (2-phenylethyl)pyrimidine-4- carboxamide	368	A
13		N-(4-fluorobenzyl)-5,6-dihydroxy-2- (3-phenylpropyl)pyrimidine-4- carboxamide	382	A

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14 OH OH OH NACO	N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-(thien-2-ylmethyl)pyrimidine-4-carboxamide	402	A
15 OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {[(morpholin-4- ylacetyl)amino]methyl}pyrimidine- 4-carboxamide (TFA salt)	420	I
16 OH OH	2-[(benzoylamino)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	397	I
17 OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (morpholin-4-ylmethyl)pyrimidine- 4-carboxamide (TFA salt)	363	E
18	benzyl 2-(4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2- yl)ethylcarbamate	441	A
19 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2-[2-(benzoylamino)ethyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	411	· I
20 OH OH OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2 methylpyrimidine-4-carboxamide	2- 278	A

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Г	21	OH OH	2-{[(N,N-	378	I
			dimethylglycyl)amino]methyl}-N-(4		1
1		"C" CONTROL O	fluorobenzyl)-5,6-		
		ا مي ة	dihydroxypyrimidine-4-	Į.	
			carboxamide (TFA salt)	ļ	1
1			carboxamide (TFA sait)		1
1		Ţ			· .
L					_[
1	22	он	2-(benzyloxycarbonylaminomethyl)-	439	A
1			N-(3-methoxybenzyl)-5,6-	-	
İ		I Charly Mark Took	dihydroxypyrimidine-4-		l
			carboxamide		1
1					
1		•,•			1
<u>_</u>					<u> </u>
	23	)	2-(benzyloxycarbonylaminomethyl)-	443	A.
			N-(4-chlorobenzyl)-5,6-		ŀ
1			dihydroxypyrimidine-4-	•	
		ŏ "	carboxamide		
1					
$\vdash$					
	24	I ou .	2-(benzyloxycarbonylaminomethyl)-	453	A
1			N-(1,3-benzodioxol-5-ylmethyl)-5,6		
	. 1		dihydroxypyrimidine-4-		1 . 1
1		. 6	carboxamide		
İ					
1		. •			
-	-				
	25	<u> </u>	2-(benzyloxycarbonylaminomethyl)-	457	A
			N-(3-chloro-4-methylbenzyl)-5,6-		i i
İ			dihydroxypyrimidine-4-		
1		ð	carboxamide		
,					
	I	•	[*		
-	26	OH.	N,2-dibenzyl-5,6-	336	$\vdash \downarrow \vdash$
1	40	A Joh A		230	A .
1			dihydroxypyrimidine-4-		
1		~~~~	carboxamide		
	ļ	0			
	- 1	*	1		
1	1	•			
	27	он	2-benzyl-N-(2-ethoxybenzyl)-5,6-	380	A
	-	04	dihydroxypyrimidine-4-	333	
	- 1		carboxamide		
1			Car Covaring C		
	-	° °			
		o,	i		1
		•			

28	CONTRACTOR ONLY	2-(1,3-benzodioxol-5-ylmethyl)-N- 3-chloro-4-methylbenzyl)-5,6- lihydroxypyrimidine-4- carboxamide	428	A
29	. ↑ AH ∧F	2-(1,3-benzodioxol-5-ylmethyl)-N- (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	398	A
30		2-(1,3-benzodioxol-5-ylmethyl)-N- (2-ethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	424	A
31	OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (thien-2-ylmethyl)pyrimidine-4- carboxamide	360	A
32		N-(3-chloro-4-methylbenzyl)-5,6-dihydroxy-2-(thien-3-ylmethyl)pyrimidine-4-carboxamide	390	A
33		N-(4-fluorobenzyl)-5,6-dihydroxy-2- (thien-3-ylmethyl)pyrimidine-4- carboxamide	360	A
3	4 CH OH OH OH	2-butyl-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	320	A

<u> </u>		Dr. (0. 13. 4		<del></del>
35	) J. OH ~ OH .	N-(3-chloro-4-methylbenzyl)-5,6-	398	A
		dihydroxy-2-(2-		
1		phenylethyl)pyrimidine-4-	ł	
		carboxamide		l
1			1	
36	OH	N-(2-ethoxybenzyl)-5,6-dihydroxy-	394	. A
1 30	ОН	2-(2-phenylethyl)pyrimidine-4-	1 3,74	. 🕰
		carboxamide		
		Carboxaniac	ļ.	
	J.			
37	<del>о</del> н	N-benzyl-5,6-dihydroxy-2-(3-	364	A
		phenylpropyl)pyrimidine-4-	.	
		carboxamide		,
1	.			
	,	1		•
38	OH .	N-benzyl-5,6-dihydroxy-2-(2-	350	A
38	,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,	phenylethyl)pyrimidine-4-	220	A.
		carboxamide		
		Carboxamide		
L	·			
39	OH .	2-(benzyloxycarbonylaminomethyl)-	453	A
`		N-(2-ethoxybenzyl)-5,6-	ł	
		dihydroxypyrimidine-4-		
	" " "	carboxamide		
			. [	
			1	*
40	OH ·	N-benzyl-5,6-dihydroxy-2-	352	<u>A</u>
"	J. OH	(phenoxymethyl)pyrimidine-4-	ا عدد	A
		carboxamide	1	
		Carooxanude	. 1	
			1	
	~		- 1	
41		NO bis/1 2 bearediesel 5	424	A
41	он 1 ж.	N,2-bis(1,3-benzodioxol-5-	727	
41		ylmethyl)-5,6-dihydroxypyrimidine-	724	
41	1		724	
41	1	ylmethyl)-5,6-dihydroxypyrimidine-	12.4	
41	1	ylmethyl)-5,6-dihydroxypyrimidine-	724	
41	1	ylmethyl)-5,6-dihydroxypyrimidine-	-2-	
	1	ylmethyl)-5,6-dihydroxypyrimidine- 4-carboxamide		
42	1	ylmethyl)-5,6-dihydroxypyrimidine- 4-carboxamide N-(4-chlorobenzyl)-5,6-dihydroxy-2	384	A
	1	ylmethyl)-5,6-dihydroxypyrimidine- 4-carboxamide  N-(4-chlorobenzyl)-5,6-dihydroxy-2 (2-phenylethyl)pyrimidine-4-		A
	1	ylmethyl)-5,6-dihydroxypyrimidine- 4-carboxamide N-(4-chlorobenzyl)-5,6-dihydroxy-2		A
	1	ylmethyl)-5,6-dihydroxypyrimidine- 4-carboxamide  N-(4-chlorobenzyl)-5,6-dihydroxy-2 (2-phenylethyl)pyrimidine-4-		A
	1	ylmethyl)-5,6-dihydroxypyrimidine- 4-carboxamide  N-(4-chlorobenzyl)-5,6-dihydroxy-2 (2-phenylethyl)pyrimidine-4-		A
	1	ylmethyl)-5,6-dihydroxypyrimidine- 4-carboxamide  N-(4-chlorobenzyl)-5,6-dihydroxy-2 (2-phenylethyl)pyrimidine-4-		A

		N-(1,3-benzodioxol-5-ylmethyl)-5,6	394	A
43	or or	dihydroxy-2-(2-		1
		phenylethyl)pyrimidine-4-	1	-
		carboxamide		ļ
ļ		CIT O O ALLES		1
- 1			-	- 1
l		N-(1,3-benzodioxol-5-ylmethyl)-5,6	386	A
44	OH	N-(1,3-benzodioxoi-3-yillicutyi) 3,5		
		dihydroxy-2-(thien-3- ylmethyl)pyrimidine-4-carboxamide		
- 1		yimethyi)pyrimidile——carooxaan	į	1
- 1	ö			ſ
		1	1	ŀ
1			250	
45	<b>О</b> Н	2-butyl-N-(3-chloro-4-	350	A
77	N CYCH	methylbenzyl)-5,6-		
- 1	HC NO O	dihydroxypyrimidine-4-	1	,
- 1	"	carboxamide		
		1	1	
	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	376	E
46	H,C, COH OF	((4-methylpiperazin-1-		
		yl)methyl]pyrimidine-4-		
	l ~ ~ » l	carboxamide (TFA salt)	1	
		1	1	
			ļ	
		N-(4-fluorobenzyl)-5,6-dihydroxy-2-	347	E
47	] OH ~ #	(pyrrolidin-1-ylmethyl)pyrimidine-4	- 1	
		carboxamide (TFA salt)		
		Carboxamide (11115ans)		
	°		}	
	1	1		
		O ( When shall N (4	369	E
48	OH	2-(anilinomethyl)-N-(4-	"	
		fluorobenzyl)-5,6-		
		dihydroxypyrimidine-4-		
	\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \	carboxamide (TFA salt)		
		D 37/4	414	A
4	9 9 9	2-(3,4-dimethoxybenzyl)-N-(4-	414	Α.
	HE ON HOW ON	fluorobenzyl)-5,6-		
		dihydroxypyrimidine-4-		
Ì	ل لم ة	carboxamide	1	
	1		1	
			1-2-	<del></del>
-	60 он	N-benzyl-5,6-dihydroxy-2-(thien-3-	342	A
1 3	S NOH	ylmethyl)pyrimidine-4-carboxamid	1	
1			1	
				i
	1		1	

	- <u></u>			
5	١	N-(2-ethoxybenzyl)-5,6-dihydroxy-	386	A
1		2-(thien-3-ylmethyl)pyrimidine-4-		1
		carboxamide		1
	45.0			
1			}	
1				
52	ун	N-(4-chlorobenzyl)-5,6-dihydroxy-2	376	A
	ST POM	(thien-3-ylmethyl)pyrimidine-4-	3,13	
		carboxamide		
1				1 .
1.			• .	
	å			
53	ÓН	2-(2,2-dimethoxyethyl)-N-(4-	352	A
	H,C N OH NF	fluorobenzyl)-5,6-	332	A .
1	HC N	dihydroxypyrimidine-4-		ľ
1	"	carboxamide		1
				] .
1.				
54	QH .	2-[(acetylamino)methyl]-N-(4-	335	7
~	OH OF	fluorobenzyl)-5,6-	333	I
1	Handle Hall	dihydroxypyrimidine-4-		
		carboxamide		
	· ·			
55	CH	N (2.2 4; 4 1) 5.6	40.4	
1 33	OH OH	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(3-	424	A
	I had an	phenylpropyl)pyrimidine-4-		
	ا لم لم	carboxamide		
	• •	ou commission		
56	O ₂	2 (han-damaaha da da da da da da da da da da da da da	400	
30	Jan A	2-(benzyloxycarbonylaminomethyl)-	409	. A
	[lantInt]	N-benzyl-5,6-dihydroxypyrimidine- 4-carboxamide		
	1. A. A. A.	Catouxamine		
			. [	
		1	ł	
	<u> </u>			
57	OH OH	2-(benzyloxycarbonylaminomethyl)-	439	A
] . [	Quillell	N-(2-methoxybenzyl)-5,6-		.
	l . M l . L	dihydroxypyrimidine-4-	ı	1
	GÇ.	carboxamide	1	
			l	1
<u>                                     </u>				
58	о ^н .он .	2-(benzyloxycarbonylaminomethyl)-	477	A
	Quillil	N-(2-trifluoromethylbenzyl)-5,6-		
•	· · l · · l · l ·	dihydroxypyrimidine-4-		
	~ .* <b>}</b> *	carboxamide		
	•		1	i
				·

59	OH CONS	2-benzyl-N-(2,3-dimethoxybenzyl)- 5,6-dihydroxypyrimidine-4- carboxamide	396	A
60		N-(1,3-benzodioxol-5-ylmethyl)-2- benzyl-5,6-dihydroxypyrimidine-4- carboxamide	380	<b>A</b>
61	HLC OH OH	N-benzyl-2-(3,4-dimethoxybenzyl)- 5,6-dihydroxypyrimidine-4- carboxamide	396	A
62	HE	N-(3-chloro-4-methylbenzyl)-2-(3,4-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	444	A
63	MC CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CALL TO CAL	2-(3,4-dimethoxybenzyl)-N-(2-ethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	440	A
64	45° X X X X X X X X X X X X X X X X X X X	N-(1,3-benzodioxol-5-ylmethyl)-2- (3,4-dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	440	A
65		2-(1,3-benzodioxol-5-ylmethyl)-N-benzyl-5,6-dihydroxypyrimidine-4-carboxamide	380	A
66		2-(1,3-benzodioxol-5-ylmethyl)-N- [4-fluoro-3-(trifluoromethyl)benzyl] 5,6-dihydroxypyrimidine-4- carboxamide	466	A

67		N-(2,4-dimethoxybenzyl)-5,6- dihydroxy-2-(2- phenylethyl)pyrimidine-4- carboxamide	410	A
68	*** A	5,6-dihydroxy-N-(3-methoxybenzyl) 2-	380	A
		(2-phenylethyl)pyrimidine-4- carboxamide		
-				
69		5,6-dihydroxy-N-(3-methoxybenzyl) 2-(thien-3-ylmethyl)pyrimidine-4- carboxamide	372	A
		.,		
70	3 N N N N	N-(2,4-dimethoxybenzyl)-5,6- dihydroxy-2-(thien-3-	402	<b>A</b> .
		ylmethyl)pyrimidine-4-carboxamide		·
71	HC CH CH	N-benzyl-2-butyl-5,6- dihydroxypyrimidine-4- carboxamide	302	A
72	OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	398	I
		[(isonicotinoylamino)methyl]pyrimi dine-4-carboxamide (TFA salt)	J70	I.
73	HC M N N F	2-[(dimethylamino)methyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	321	С
74	QH	2-(1,3-benzodioxol-5-ylmethyl)-5,6-	410	
/**		dihydroxy-N-(3- methoxybenzyl)pyrimidine-4- carboxamide	410	A

412	A
293	A*
- 469	A
440	A
410	A
402	A
275	M
362	A
_	302

	<u> </u>			
83	HC CH CH CH	N-(2,3-dimethoxybenzyl)-2-(3,4-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	456	A
84	H,C, OH, OH, OH, OH, OH, OH, OH, OH, OH, OH	N-(2,3-dimethoxybenzyl)-2-(2,2-dimethoxyethyl)-5,6-dihydroxypyrimidine-4-carboxamide	394	A
85		N-(4-fluorobenzyl)-5,6-dihydroxy-2- ({[(4-methylpiperazin-1- yl)acetyl]amino}methyl)pyrimidine- 4-carboxamide (TFA salt)	433	I
86		2-benzyl-N-(4-fluorobenzyl)-5- hydroxy-6-(2-morpholin-4- ylethoxy)pyrimidine-4-carboxamide (TFA salt)	467	J
87		2-benzyl-6-[2- (dimethylamino)ethoxy]-N-(4- fluorobenzyl)-5-hydroxypyrimidine- 4-carboxamide (TFA salt)	425	J

able 11		N-(4-fluorobenzyl)-5,6-dihydroxy-2-	363	C
1	ON NOT F	(4-methylmorpholin-2- yl)pyrimidine-4-carboxamide (TFA salt)		
2	ĊH,	2-[4-(N,N-	434	I
		dimethylglycyl)morpholin-2-yl]-N- (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)		
3 ну	CH OH OH	2-(diethoxymethyl)-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	366	A
4	OH OH OH	N-benzyl-5,6-dihydroxy-2- [methoxy(phenyl)methyl]pyrimidine 4-carboxamide	366	A
5	GC-O-N-OH-OH-O-O-O-G	5,6-dihydroxy-N-(3-methoxybenzyl) 2- [methoxy(phenyl)methyl]pyrimidine 4-carboxamide		A
6	H,C. Y N Y F	2-[1-(benzyloxy)butyl]-N-(3,4-difluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	444	A
7	H,C , N , CH, CH,	2-[1-(benzyloxy)butyl]-N-(3-chloro 4-methylbenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	456	A

<b>\begin{align*}</b>	a II a Da	2-[(benzyloxy)(phenyl)methyl]-N- (2,3-dimethoxybenzyl)-5,6- dihydroxynyzimidine.4	502	A
	A Land &	dihydroxypyrimidine-4- carboxamide		
	· ·			
g	OH OH	2-[(benzyloxy)(phenyl)methyl]-N-(4 fluorobenzyl)-5,6-	460	A
		dihydroxypyrimidine-4- carboxamide	:	
10	OH OH OH,	2-[(benzyloxy)(phenyl)methyl]-N-(3 chloro-4-methylbenzyl)-5,6-	490	A
		dihydroxypyrimidine-4- carboxamide	٠	
12	OH OH	N-(2,3-dimethoxybenzyl)-5,6-	426	A
	O I NO OR	dihydroxy-2- [methoxy(phenyl)methyl]pyrimidine		
	HC 0 0 0'OH	4-carboxamide		
			, .	
13	H,C' OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [methoxy(phenyl)methyl]pyrimidine 4-carboxamide	384	A
14	OH OH COL	N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2- [methoxy(phenyl)methyl]pyrimidine	414	. <b>A</b>
		4-carboxamide		-
15	1	N-benzyl-5,6-dihydroxy-2-(1-	318	A*
	H.C. OH	hydroxybutyl)pyrimidine-4- carboxamide		
	Сн. " И			
16	OH OH	N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2-(1-	366	A*
	HC OH NOTO	hydroxybutyl)pyrimidine-4- carboxamide		
	·			

	·		226: 1	1 *
17	JOH OF	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (1-hydroxybutyl)pyrimidine-4- carboxamide	336	A*
18	to III	2-[1-(benzyloxy)butyl]-5,6- dihydroxy-N-(3- methoxybenzyl)pyrimidine-4- carboxamide	438	A
19	H _L C OH OH OH	N-(1,3-benzodioxol-5-ylmethyl)-5,6-dihydroxy-2- [methoxy(phenyl)methyl]pyrimidine 4-carboxamide	410	A
20	H,C , OH , OCI,	2-[1-(benzyloxy)butyl]-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	468	A
21	OH OH FF	2-[(benzyloxy)(phenyl)methyl]-N-[4 fluoro-3-(trifluoromethyl)benzyl]- 5,6-dihydroxypyrimidine-4- carboxamide	528	A
22	H,C O H OH OH	N-(4-chlorobenzyl)-5,6-dihydroxy-2 [methoxy(phenyl)methyl]pyrimiding 4-carboxamide	400	A
23	H,C OH OH OH,	5,6-dihydroxy-N-(2-methoxybenzy) 2- [methoxy(phenyl)methyl]pyrimidin 4-carboxamide		A

	·			
24	1	N-[4-fluoro-3-	452	A
1	N OH F	(trifluoromethyl)benzyl]-5,6-		
1	HC O N N F	dihydroxy-2-		
1	] "   F	[methoxy(phenyl)methyl]pyrimidine		
1		4-carboxamide		
				İ
<u></u>				ļ
25	OH	N-(3,4-difluorobenzyl)-5,6-	402	A.
ŀ	N OH OH	dihydroxy-2-		1 .
	HC Q N N N N N N N N N N N N N N N N N N	[methoxy(phenyl)methyl]pyrimidine		-
1 .		4-carboxamide		
		1	٠.	ł
1	~	· 1		ļ
26	OH	N-(2,3-dimethoxybenzyl)-5,6-	378	A*
~~	HO.	dihydroxy-2-(1-	3/6	A
1	Inc. II n II m	hydroxybutyl)pyrimidine-4-		
	I ~ L ~ L ~ L ~ L ~ .	carboxamide		
	⁰⁴	Carooxamide		
				,
L				
27	OН	5,6-dihydroxy-2-(1-hydroxybutyl)-N	348	A*
ļ	N, → OH	(3-methoxybenzyl)pyrimidine-4-		
1	HC A CON	carboxamide		•
1.	H H			
28	A4	tert-butyl 2-(4-{[(4-	440	
20	J. 04		449	A
		fluorobenzyl)amino]carbonyl}-5,6-		
· [		dihydrexypyrimidin-2-	,	,
	, N	yl)morpholine-4-carboxylate		:
	مر م			
•	HC OL			
	•			
29	ÒН	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	349	A*
	OH F	morpholin-2-ylpyrimidine-4-		
		carboxamide (TFA salt)		ı
			,	
	\ <u>\</u> \		į	
			.	
20		N. (2	415	
30	OH A	N-(2-ethoxybenzyl)-5,6-dihydroxy-	410	A
		2-	!	
	Hc ~ ~ ~	[methoxy(phenyl)methyl]pyrimidine		j
		4-carboxamide		- 1
	L		. [	
	~ '	·		i

31	00001110000	benzyl 4-[(benzyloxy)(4-{[(2,3-dimethoxybenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)methyl]piperidine-1-carboxylate	643	A
32	THE CHAIN COLL	2-[(benzyloxy)(piperidin-4- yl)methyl]-N-(2,3-dimethoxybenzyl) 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	509	A*

Table 12	OH OH CH,	N-(3-chloro-4-methylbenzyl)-5,6-dihydroxy-2-isopropylpyrimidine-4-carboxamide	336	A
	OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (1-phenylethyl)pyrimidine-4- carboxamide	368	A
3	OH OH CH,	N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2-(1- phenylethyl)pyrimidine-4- carboxamide	398	A
4	OH OH FF	N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-(1- phenylethyl)pyrimidine-4- carboxamide	436	A
5 4,0	OH OH F	N-(3,4-difluorobenzyl)-5,6-dihydroxy-2-isopropylpyrimidine-4-carboxamide	324	A

	•	•		
	CH, OH	N-benzyl-5,6-dihydroxy-2-(1- phenylethyl)pyrimidine-4- carboxamide	350	A
7	OH OH OH	N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-(1-phenylethyl)pyrimidine-4- carboxamide	394	A
8	OH OH OH OH,	N-(2,4-dimethoxybenzyl)-5,6- dihydroxy-2-(1- phenylethyl)pyrimidine-4- carboxamide	410	A
9		N-(1,3-benzodioxol-5-ylmethyl)-5,6-dihydroxy-2-(1-phenylethyl)pyrimidine-4-carboxamide	394	A
10	OH, OH OH	N-(4-chlorobenzyl)-5,6-dihydroxy-2 (1-phenylethyl)pyrimidine-4- carboxamide	384	A
11	OH, WHOM ON	5,6-dihydroxy-N-(3-methoxybenzyl) 2-(1-phenylethyl)pyrimidine-4- carboxamide	380	A
12	H,C CH, OH N	N-(4-fluorobenzyl)-5,6-dihydroxy-2- isopropylpyrimidine-4-carboxamide	306	A

		V (2 2 1' - who well vi) 5.6	410	A
13	O TON O ON	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(1- phenylethyl)pyrimidine-4-	410	
	GH, " B CH,	carboxamide		
14	OH JF	N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-isopropylpyrimidine-4- carboxamide	374	A
15	↓ oH ∧	N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-isopropylpyrimidine-4- carboxamide	332	A
16	HC OH	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-isopropylpyrimidine-4- carboxamide	348	A
17	H,C H, OH OH	N-(1,3-benzodioxol-5-ylmethyl)-5,6- dihydroxy-2-isopropylpyrimidine-4- carboxamide		A
18	H ₃ C H ₃ OH	N-benzyl-5,6-dihydroxy-2- isopropylpyrimidine-4-carboxamide		A
19	H,C CH, OH FF	N-[4-fluoro-3- (trifluoromethyl)benzyl]-5,6- dihydroxy-2-isopropylpyrimidine-4- carboxamide	374	A

Г	20	ÓН		ζн,	N-(2,4-dimethoxybenzyl)-5,6-	348	A
1		ű	OH		dihydroxy-2-isopropylpyrimidine-4- carboxamide		
1		H _s C	~N~	<b>├</b> .			ī
		ĊН	Ö	γ [′] cH′			
	- 1		•				

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Table 13			
1 OH	N-benzyl-2-cyclopentyl-5,6- dihydroxypyrimidine-4-	314	A
	carboxamide		
2 OH , CH,	N-(3-chloro-4-methylbenzyl)-2- cyclopentyl-5,6-	362	A
	dihydroxypyrimidine-4-		
	carboxamide		_
3 OH OF	2-cyclopentyl-N-(4-fluorobenzyl)- 5,6-dihydroxypyrimidine-4-	332	A
	carboxamide		
4 OH OH	2-cyclopentyl-N-(2,3-dimethoxybenzyl)-5,6-	374	A
I No as	dihydroxypyrimidine-4- carboxamide		
d day	carooxamide		
5 OH	2-cyclopentyl-N-(2-ethoxybenzyl)- 5,6-dihydroxypyrimidine-4-	358	A
	carboxamide		
ભ			:
6 OH OF	2-cyclopentyl-N-[4-fluoro-2- (trifluoromethyl)benzyl]-5,6-	400	A
	dihydroxypyrimidine-4-		
\\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\	carboxamide		
	·		

7	OH	2-cyclopentyl-5,6-dihydroxy-N-(2- methoxybenzyl)pyrimidine-4- carboxamide	344	A
8	OH OH CO	N-(1,3-benzodioxol-5-ylmethyl)-2- cyclopentyl-5,6- dihydroxypyrimidine-4- carboxamide	358	A
9	OH NO CH,	2-cyclopentyl-5,6-dihydroxy-N-(3-methoxybenzyl)pyrimidine-4-carboxamide	344	A
10	OH OH, OH,	2-cyclopentyl-N-(2,4- dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	374	A

Table	OH OH CF	N-(3,4-difluorobenzyl)-5,6- dihydroxy-2-[morpholin-4- yl(phenyl)methyl] pyrimidine-4-carboxamide (TFA salt)	457	В
2	OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [morpholin-4- yl(phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)	439	В
3	H ₃ C ^N CH ₃	2-[(dimethylamino)(phenyl)methyl]- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	397	В

. 4	OH OH OF	N-(4-fluorobenzyl)-5,6-dihydroxy-2 [(2-methyl-2,3-dihydro-1H-indol-1- yl)(phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)		В
	D'ai,			
5		N-(4-fluorobenzyl)-5,6-dihydroxy-2 {phenyl[(pyridin-3- ylmethyl)amino]methyl}pyrimidine- 4-carboxamide (TFA salt)	460	В.
	6	(1177 3416)		
6	H,C-N, CH, OH OH OH	N-(3,5-dichlorobenzyl)-2- [(dimethylamino)(phenyl)methyl]- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	447	В
7		N-(4-fluorobenzyl)-2-[(4- formylpiperazin-1- yl)(phenyl)methyl]-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	466	В
8		N-(4-fluorobenzyl)-5,6-dihydroxy-2- [{[3-(1H-imidazol-1- yl)propyl]amino} (phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)	477	В
9		N-(4-fluorobenzyl)-2-[[(4-fluorobenzyl)amino](phenyl)methyl]-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)	477	В
10		N-(4-fluorobenzyl)-5,6-dihydroxy-2- [(4-methylpiperazin-1- yl)(phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)	452	В

11		2-[[(3,4-dimethoxybenzyl)amino] (phenyl)methyl]-N-(4-fluorobenzyl)- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	519	В
12	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [(2-methyl-2,3-dihydro-1H-indol-1- yl)(phenyl)methyl]pyrimidine-4-	485	В
13	OH OH	carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- [[4-(2-methoxyphenyl)piperazin-1-	544	В
		yl](phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)		
14	OH OH OH	N-(2,4-difluorobenzyl)-2- [(dimethylamino)(phenyl)methyl]- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	415	В
15	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2 {phenyl[(pyridin-4- ylmethyl)amino]methyl}pyrimidine- 4-carboxamide (TFA salt)	1	В
16	OH OH	N-(3,4-difluorobenzyl)-5,6-dihydroxy-2-[phenyl(piperidin-1-yl)methyl]pyrimidine-4-carboxamide (TFA salt)	455	В
1	7 OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-; [phenyl(piperidin-1- yl)methyl]pyrimidine-4- carboxamide (TFA salt)	2 437	В .

N-(4-fluorobenzyl)-5,6-dihydroxy-2 494    19			Ja son i i i i i i i i i i i i i i i i i i i	т	т
N-(4-fluorobenzyl)-5,6-dihydroxy-2 494  [{[3-(2-oxopyrrolidin-1-y0)propyl]amino}([phenyl])methyl]pyrimidine-4-carboxamide (TFA salt)    N-(4-fluorobenzyl)-5,6-dihydroxy-2 512 [{[2-(1H-indol-3-y0)ethyl]amino}(phenyl)methyl]pyrimidine-4-carboxamide (TFA salt)    N-(4-fluorobenzyl)-5,6-dihydroxy-2 512 [{[2-(1H-indol-3-y0)ethyl]amino}(phenyl)methyl]pyrimidine-4-carboxamide (TFA salt)    N-(4-fluorobenzyl)-5,6-dihydroxy-2 fli(25)-2-(methoxymethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)    N-(4-fluorobenzyl)-5,6-dihydroxy-2 fli(25)-2-(methoxymethyl)pyrrolidin-1-y1](phenyl)methyl]pyrrimidine-4-carboxamide (TFA salt)    N-(4-fluorobenzyl)-5,6-dihydroxy-2 fli(25)-2-(methoxymethyl)pyrrolidin-1-y1](phenyl)methyl]pyrrimidine-4-carboxamide (TFA salt)	18	l	dihydroxypyrimidine-4-	397	В
Compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to the compared to		H _G C-N CH,	carboxamide		
[{[2-(1H-indol-3-yl)ethyl]amino}(phenyl)methyl]pyrimidine-4-carboxamide (TFA salt)  2- [[benzyl(methyl)amino](phenyl)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)  22  2- [1,4-dioxa-8-azaspiro[4.5]dec-8-yl(phenyl)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)  23  3- 3- 495 3- 495 3- 467 467 467 467 468 468 495 495 495 495 495 495 495 495 495 495	19	1	[{[3-(2-oxopyrrolidin-1-yl)propyl]amino}(phenyl)methyl]py	ĺ	В
Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Charles   Char		<b>_</b> 0			
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[[benzyl(methyl)amino](phenyl)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)  22		<b>N</b>			
yl(phenyl)methyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- [[(2S)-2-(methoxymethyl)pyrrolidin- 1-yl](phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- 460 {phenyl[(pyridin-2- ylmethyl)amino]methyl}pyrimidine-	21	HC Y	[[benzyl(methyl)amino](phenyl)met hyl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-	473	В
yl(phenyl)methyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- [[(2S)-2-(methoxymethyl)pyrrolidin- 1-yl](phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- 460 {phenyl[(pyridin-2- ylmethyl)amino]methyl}pyrimidine-					
23  OH  Chies  N-(4-fluorobenzyl)-5,6-dihydroxy-2-467  [[(2S)-2-(methoxymethyl)pyrrolidin-1-yl](phenyl)methyl]pyrimidine-4-carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2-460  {phenyl[(pyridin-2-ylmethyl)amino]methyl}pyrimidine-	22		yl(phenyl)methyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4-	495	В
[[(2S)-2-(methoxymethyl)pyrrolidin- 1-yl](phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)  N-(4-fluorobenzyl)-5,6-dihydroxy-2- {phenyl[(pyridin-2- ylmethyl)amino]methyl}pyrimidine-		*	carboxamide (TFA salt)		
24 OH N-(4-fluorobenzyl)-5,6-dihydroxy-2 460 {phenyl[(pyridin-2-ylmethyl)amino]methyl}pyrimidine-	23	4	[[(2S)-2-(methoxymethyl)pyrrolidin- 1-yl](phenyl)methyl]pyrimidine-4-	467	В
{phenyl[(pyridin-2-ylmethyl)amino]methyl}pyrimidine-	·	#c~\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	Carboxamide (1FA sait)		
N^	24		{phenyl[(pyridin-2- ylmethyl)amino]methyl}pyrimidine-	460	В

		, , , , , , , , , , , , , , , , , , ,	480	В
25	OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {phenyl[(2-piperidin-1- ylethyl)amino]methyl}pyrimidine-4- carboxamide (TFA salt)	480	B
26		N-(4-fluorobenzyl)-5,6-dihydroxy-2- [[(3-morpholin-4- ylpropyl)amino](phenyl)methyl]pyri	496	В
		midine-4-carboxamide (TFA salt)	421	В
27	OH OH OH	N-benzyl-5,6-dihydroxy-2- [morpholin-4- yl(phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)	421	В
28	OH OH OH F	2-[(dimethylamino)(phenyl)methyl]- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	397	В .
29	OH Chical  OH  Chical  CH ₃ F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [{[(1S)-1- methylpropyl]amino}(phenyl)methy l]pyrimidine-4-carboxamide (TFA salt)	425	В
3	OH OH OH F	N-(3,4-difluorobenzyl)-5,6-dihydroxy-2-[(4-methylpiperazin-1-yl)(phenyl)methyl]pyrimidine-4-carboxamide (TFA salt)	470	В
3	1 OH OH	N-(2-ethoxybenzyl)-5,6-dihydroxy- 2-[morpholin-4- yl(phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)	465	В

32	OH .	N-(2,3-dimethoxybenzyl)-5,6-	494	В
	M M M	dihydroxy-2-[(4-methylpiperazin-1-		
. [	N N ON	yl)(phenyl)methyl]pyrimidine-4-		
		carboxamide (TFA salt)		
	н,с-		.	
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		N (40) 0.2 dibadas 1H index 1 all	405	В
33	OH Chiral	N-[(1S)-2,3-dihydro-1H-inden-1-yl]-	403	<b>D</b> .
	N OH	2-[(dimethylamino)(phenyl)methyl]-	· .	
		5,6-dihydroxypyrimidine-4-	1	
		carboxamide (TFA salt)		
	HC N CH O			
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34	ОН	N-(2-chlorobenzyl)-2-	413	В
54	<b>.</b>	[(dimethylamino)(phenyl)methyl]-		
	N OH	5,6-dihydroxypyrimidine-4-		
!	しょ			
٠.		carboxamide (TFA salt)	]	
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•	•			
35	ОН	N-(3,4-difluorobenzyl)-2-	415	В
-		[(dimethylamino)(phenyl)methyl]-		
		5,6-dihydroxypyrimidine-4-		
•		carboxamide (TFA salt)	Ī	
		carooxamide (11'A sait)		
	ңс ^л оң			
36	<b>о</b> н	2-[(dimethylamino)(phenyl)methyl]-	409	В
	OH OH	5,6-dihydroxy-N-(3-	Į	
		methoxybenzyl)pyrimidine-4-	ļ	
		carboxamide (TFA salt)	1	
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		NI (4 Flygge barged) 5 6 dibydgayy 2	482	В
37	) oH <	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	404	D
		[[(2-morpholin-4-		
		ylethyl)amino](phenyl)methyl]pyri		
		midine-4-carboxamide (TFA salt)	l	
		l i		
	( `N		- 1	
	$\sim$		- 1	
38	OH-	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	466	В
30	OH OF	{phenyl[(2-pyrrolidin-1-		-
		ylethyl)amino]methyl}pyrimidine-4-	- 1	
	ة ش _{م .} ا	carboxamide (TFA salt)	ļ	
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39		N-(4-fluorobenzyl)-5,6-dihydroxy-2- [{[(1R)-1- (hydroxymethyl)propyl]amino}(phe nyl)methyl]pyrimidine-4- carboxamide (TFA salt)	441	В
40	OH OH OH F	2-[(diethylamino)(phenyl)methyl]-N (3,4-difluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	443	В
41	OH OH OH OH OH	2-[(diethylamino)(phenyl)methyl]-N (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	425	В
42		2-[(4-benzylpiperazin-1- yl)(phenyl)methyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	528	В
4	3 OH OH OH OH	N-benzyl-2- [(dimethylamino)(phenyl)methyl]- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	379	В
	4 OH OH OH OH OH OH OH OH OH OH OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [[methyl(1-methylpiperidin-4- yl)amino](phenyl)methyl]pyrimidin e-4-carboxamide (TFA salt)	480	В
	45 OH OH OH H,C N	N-(4-fluorobenzyl)-5,6-dihydroxy-2 [(2-methylpyrrolidin-1- yl)(phenyl)methyl]pyrimidine-4- carboxamide (TFA salt)	437	В

46	OH OH	N-(2,3-dimethoxybenzyl)-5,6-	481	В
	OH OH	dihydroxy-2-[morpholin-4-		
		yl(phenyl)methyl]pyrimidine-4-	1	
	I N I V YOU'S	carboxamide (TFA salt)	1.	
	ا ر م م	Carboxamuce (11'A sait)		ĺ
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· <u>L</u>			<u>.</u>	1
47	ÓН	N-(2-ethoxybenzyl)-5,6-dihydroxy-	463	В
]	→ H	2-[phenyl(piperidin-1-		
1		yl)methyl]pyrimidine-4-		1
1		carboxamide (TFA salt)		1 .
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48	ОН	5,6-dihydroxy-N-(3-methoxybenzyl)	449	В
	OH OH	2-[phenyl(piperidin-1-		1
]		yl)methyl]pyrimidine-4-	,	
		carboxamide (TFA salt)		
	્રાં ઉં દેમ,	The same (11 11 sail)	•	
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<u> </u>	<u> </u>			
49	OH .	5,6-dihydroxy-N-(3-methoxybenzyl)	451	В
] -		2-[morpholin-4-	•	1
	OH, NOW OH,	yl(phenyl)methyl]pyrimidine-4-		
		carboxamide (TFA salt)		
<b>!</b>				
<del> </del> _	, au	77 (4 5)	70.5	
50	OH Chiral	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	506	В
		{phenyl[(2S)-2-(pyrrolidin-1-	j	·
		ylmethyl)pyrrolidin-1-		
	~ " "	yl]methyl}pyrimidine-4-		
- 1		carboxamide (TFA salt)		
	·	·		
. 51	OH	N (2.2 dimethousehousel) 5.5	470	
. 51		N-(2,3-dimethoxybenzyl)-5,6-	479	В .
.		dihydroxy-2-[phenyl(piperidin-1-		·
- 1	N N N N N N N N N N N N N N N N N N N	yl)methyl]pyrimidine-4-		
.	,	carboxamide (TFA salt)		'
- 1	H _C C CA		, 1	
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- 1				
52	OH ·	5,6-dihydroxy-N-(3-methoxybenzyl)	464	В
32	Λ J OH Λ		404	D
		2-[(4-methylpiperazin-1-		. 1
		yl)(phenyl)methyl]pyrimidine-4-	- 1	
1	, i ö	carboxamide (TFA salt)	ŀ	
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53		2-[[(4- fluorobenzyl)amino](phenyl)methyl ]-5,6-dihydroxy-N-(pyridin-2- ylmethyl)pyrimidine-4-carboxamide (TFA salt)	460	В
54	CH, OH OH OH, OCH, OCH,	N-(2,3-dimethoxybenzyl)-2- [(dimethylamino)(phenyl)methyl]- 5,6-dihydroxypyrimidine-4- carboxamide (TFA salt)	439	В
55	OH OH	2-[[(4-fluorobenzyl)amino](phenyl)methyl]-5,6-dihydroxy-N-(pyridin-3-ylmethyl)pyrimidine-4-carboxamide (TFA salt)		В
56		5,6-dihydroxy-2-{phenyl[(pyridin-2-ylmethyl)amino]methyl}-N-(pyridin 2-ylmethyl)pyrimidine-4-carboxamide (TFA salt)		В
57	OH OH OH OH, O CH, OH, CH, CH, CH, CH, CH, CH, CH, CH, CH, C	2-[(diethylamino)(phenyl)methyl]-N (2,3-dimethoxybenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	467	В

Table 15	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {1-methyl-1-[(pyridin-2- ylcarbonyl)amino]ethyl}pyrimidine- 4-carboxamide (TFA salt)	426	I
2 OH OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- { 1-[(pyridin-2- ylcarbonyl)amino]cyclohexyl}pyrim idine-4-carboxamide (TFA salt)	466	I

3	ÓН	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	448	I
	N OH OF	{1-methyl-1-[(morpholin-4-		
		ylacetyl)amino]ethyl)pyrimidine-4-	i	
	MILLO ON TO S	carboxamide (TFA salt)		
	ه و مود عود ا	Carooxamido (1111 saity	- 1	
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	ОН	2-[1-(acetylamino)cyclohexyl]-N-(4-	403	I
4	l			•
	N OH F	fluorobenzyl)-5,6-		
	HC N L L N L	dihydroxypyrimidine-4-	·	
		carboxamide		
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- 1				
5	ОН	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	335	С
	↓ OH	[1-methyl-1-	. [	
		(methylamino)ethyl]pyrimidine-4-	1	
			. 1	
	HC CH X	carboxamide	1	* •
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6	o^COL,	N-(4-fluorobenzyl)-5-hydroxy-6-	440	I
١	)	methoxy-2-{1-methyl-1-[(pyridin-2-	1	
	N N N	ylcarbonyl)amino]ethyl)pyrimidine-		
·	∬դշ^o₃" ∦	4-carboxamide (TFA salt)	l	
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		2 ft (3' - shale -i- e) and about 11 N	389	E
7	OH .	2-[1-(dimethylamino)cyclohexyl]-N-	307	E
	OH OF	(4-fluorobenzyl)-5,6-		
		dihydroxypyrimidine-4-		
<b>!</b> !	HG N Y	carboxamide (TFA salt)	. 1	
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8	φн	benzyl 1-(4-{[(4-	455	Ā
8	2 L 4 2	benzyl 1-(4-{[(4-fluorobenzyl)aminolcarbonyl}-5.6-	455	A
8	an Han	fluorobenzyl)amino]carbonyl}-5,6-	455	A
8		fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)-1-	455	A
8	Q Q N T N O	fluorobenzyl)amino]carbonyl}-5,6-	455	A
8		fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)-1-	455	<b>A</b>
8		fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)-1-	455	<b>A</b>
8		fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)-1-	455	<b>A</b>
	Charles and the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the	fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)-1- methylethylcarbamate		
8	OH OH	fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate  2-(1-aminocyclohexyl)-N-(4-	455	A*
	Charles and the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the second of the	fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate  2-(1-aminocyclohexyl)-N-(4-fluorobenzyl)-5,6-		
	OH OH	fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate  2-(1-aminocyclohexyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-		
	OH OH	fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate  2-(1-aminocyclohexyl)-N-(4-fluorobenzyl)-5,6-		
	OH OH	fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate  2-(1-aminocyclohexyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-		
	OH OH	fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate  2-(1-aminocyclohexyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-		
	OH OH	fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate  2-(1-aminocyclohexyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-		

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			7/0	<del></del> -
10	HC CH, OH OH	2-[1-(dimethylamino)-1- methylethyl]-N-(4-fluorobenzyl)-5,6 dihydroxypyrimidine-4- carboxamide (TFA salt)	349	E
11	H _G C CH ₃ OH Br	N-(3-bromo-4-fluorobenzyl)-2-[1- (dimethylamino)-1-methylethyl]-5,6 dihydroxypyrimidine-4- carboxamide (TFA salt)	428	E
12		benzyl 1-(4-{[(4- fluorobenzyl)amino]carbonyl}-5- hydroxy-6-methoxypyrimidin-2-yl)- 1-methylethylcarbamate	469	J
13	OH OH H ₂ N N N N F	2-(1-amino-1-methylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	321	A*
1.	The contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract of the contract o	benzyl 1-(4-{[(2,3-dimethoxybenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethylcarbamate	497	A
1	5 OCH ₃ OH H ₂ N N N N N N F	2-(1-amino-1-methylethyl)-N-(4-fluorobenzyl)-5-hydroxy-6-methoxypyrimidine-4-carboxamide	335	A*
	6 CH ₃ N OH F	2-[1-(dimethylamino)-1- methylethyl]-N-(4-fluorobenzyl)-5- hydroxy-6-methoxypyrimidine-4- carboxamide	363	A

Table 16

	<u> </u>			
;	1  он	N-(4-fluorobenzyl)-5,6-dihydroxy-2	395	C
	N OH OH	(1-methyl-2,3-dihydro-1H-indol-2-	l	
		yl)pyrimidine-4-carboxamide (TFA		1
		salt)	1	
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	2	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	488	I
	N OH F	{2-phenyl-1-[(pyridin-2-		1
		ylcarbonyl)amino]ethyl}pyrimidine-		Į
		4-carboxamide (TFA salt)		
<b>I</b> .	I	(		j
ľ				
3	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	409	С
	∫ OH ∧ F	(2-methyl-1,2,3,4-		ľ
1	I PY	tetrahydroisoquinolin-3-	•	I
1		yl)pyrimidine-4-carboxamide (TFA		
	l l	salt)		
	- ~~			, .
1		<u> </u>		
4	OH	2-(2-benzoyl-1,2,3,4-	499	I
	OH OF	tetrahydroisoquinolin-3-yl)-N-(4-	7/7	, ×,
		fluorobenzyl)-5,6-		
		dihydroxypyrimidine-4-		
1		carboxamide		
		Catooyamde		•
İ				
5	ОН	2-[1-(N,N-dimethylglycyl)-2,3-	466	I
	OH OF	dihydro-1H-indol-2-yl]-N-(4-	700	
		fluorobenzyl)-5,6-	[	
		dihydroxypyrimidine-4-		
			. [	
	y as	carboxamide (TFA salt)	- 1	
	ĊŊ,	1.		
6	- CH	2-(2,3-dihydro-1H-indol-2-yl)-N-(4-	381	A*
	, on , r	fluorobenzyl)-5,6-	201	ΑŦ
	N Y CH			
		dihydroxypyrimidine-4-	į	
		carboxamide (TFA salt)	j	
	\ <b>_</b> /			
	. •		- 1	
7		N-(4-fluorobenzyl)-5,6-dihydroxy-2-	205	
· '	ОН		395	A*
	N OH	(1,2,3,4-tetrahydroisoquinolin-3-	l	
į		yl)pyrimidine-4-carboxamide	- 1	
· l			·	
	- N	İ		
	•		- 1	
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		D. S. G. Physhogy 2	522	T
8	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [2-(morpholin-4-ylacetyl)-1,2,3,4- tetrahydroisoquinolin-3- yl]pyrimidine-4-carboxamide (TFA	J22	
		salt)	105	I
9	SHOW OF	2-(1-benzoyl-2,3-dihydro-1H-indol- 2-yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	485	
10	CH OH CF	2-(1-benzyl-2,3-dihydro-1H-indol-2- yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	471	С
11	OH OH OH	2-[1-(dimethylamino)-2- phenylethyl]-N-(4-fluorobenzyl)-5,6 dihydroxypyrimidine-4- carboxamide (TFA salt)	411	С
1:		benzyl 2-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)indoline-1-carboxylate		A
1	3 CH OH OH OH OH OH OH OH OH OH OH OH OH OH	2-[2-(N,N-dimethylglycyl)-1,2,3,4-tetrahydroisoquinolin-3-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)	480	I
	14 OH OH OH OH OH OH OH OH OH OH OH OH OH	tert-butyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-2-phenylethylcarbamate	483	A

15	OH OH OH OH	2-{1-[(N,N-dimethylglycyl)amino]- 2-phenylethyl}-N-(4-fluorobenzyl)- 5,6-dihydroxypyrimidine-4- carboxamide	468	I
16	OH OH Z	2-(1-amino-2-phenylethyl)-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	383	A*

Table	17			
1		benzyl 2-(4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)piperidine- 1-carboxylate	481	<b>A</b> .
2	OH OH OH OH OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(methylsulfonyl)piperidin-2- yl]pyrimidine-4-carboxamide	425	I
3	OH OH OH OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {1-[(4-methyl-1,2,3-thiadiazol-5- yl)carbonyl]piperidin-2- yl}pyrimidine-4-carboxamide (TFA salt)	473	I
4	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(1H-imidazol-4- ylcarbonyl)piperidin-2- yl]pyrimidine-4-carboxamide (TFA salt)	441	1
5	OH OH OH OH OH OH OH OH OH OH OH OH OH O	2-{1-[(2,4-dimethyl-1,3-thiazol-5-yl)carbonyl]piperidin-2-yl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)	486	I

6	OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {1-[(1-methyl-1H-imidazol-2- yl)carbonyl]piperidin-2- yl}pyrimidine-4-carboxamide (TFA salt)	455	I
7		N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(pyridazin-3-ylcarbonyl)piperidin 2-yl]pyrimidine-4-carboxamide	453	I
8	CH CH CH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {1-[(4-methylmorpholin-2- yl)carbonyl]piperidin-2- yl}pyrimidine-4-carboxamide	474	I
9	OH OH OH OH	2-(1-acetylpiperidin-2-yl)-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	389	I
10		2-(1-benzoylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	451	I
11		2-[1-(anilinocarbonyl)piperidin-2- yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	466	G
1:		N-(4-fluorobenzyl)-5,6-dihydroxy-2 [1-(pyridin-2-ylcarbonyl)piperidin-yl]pyrimidine-4-carboxamide (TFA salt)	2	1

		12 22 22 22 22 22 22 22 22 22 22 22 22 2	401	<del></del>
13	OH Loh 🌣 🗲	2-[1-(1H-benzimidazol-5-	491	I
		ylcarbonyl)piperidin-2-yl]-N-(4-		•
		fluorobenzyl)-5,6-		•
		dihydroxypyrimidine-4-		
		carboxamide (TFA salt)	'	
	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\			•
-	<b>1</b>			
14	ĢН	2-{1-	418	G
	OH OF	[(ethylamino)carbonyl]piperidin-2-	1	
		yl}-N-(4-fluorobenzyl)-5,6-		
		dihydroxypyrimidine-4-		
		carboxamide	. 1	
	<b>~</b>	Carooxamide		
	Ċrţ,	·		
15	OH .	N-(4-fluorobenzyl)-2-(1-	375	I
~~	J on ∧ F	formylpiperidin-2-yl)-5,6-	- 1	
		dihydroxypyrimidine-4-		
		carboxamide	l	
		Carooxamuuc		
			٠,	
	Ö	·		•
16	OU.	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	347	A*
10	OH .	piperidin-2-ylpyrimidine-4-	- ''	
	N OH	carboxamide		
		carboxamide	- 1	
		\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	l	
	VN Ö		- 1	
		N-(4-fluorobenzyl)-5,6-dihydroxy-2-	438	D
17	I ou		450	D
		[1-(pyridin-4-ylmethyl)piperidin-2-	.	-
		yl]pyrimidine-4-carboxamide (TFA		
	<b>\</b>	salt)	- 1	
	*			
18	он	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	452	I
	, on of	(1-isonicotinoylpiperidin-2-		
		yl)pyrimidine-4-carboxamide (TFA		
		salt)		
				•
	, TV			
19	Òн	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	474	I
	N CH C	[1-(morpholin-4-ylacetyl)piperidin-		
		2-yl]pyrimidine-4-carboxamide	Ì	
		(TFA salt)		
		(II A sail)		
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20	OH OH	2-(1-ethylpiperidin-2-yl)-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	375	
21	64, CH, CH, CH, CH, CH, CH, CH, CH, CH, CH,	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(pyridin-3-ylcarbonyl)piperidin-2- yl]pyrimidine-4-carboxamide (TFA salt)	452	I
22		N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(pyridin-3-ylmethyl)piperidin-2- yl]pyrimidine-4-carboxamide (TFA salt)	438	D
23	OH OH	2-(1-benzylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)	437	D
24	THOM OF S	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(2-oxo-2-phenylethyl)piperidin-2- yl]pyrimidine-4-carboxamide (TFA salt)	465	D
2.5	OH OH OH OH, CH,	benzyl 2-(4-{[(2,3-dimethoxybenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)piperidine-1-carboxylate	523	A
2	6 OH OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2 (1-isobutylpiperidin-2-yl)pyrimidine 4-carboxamide (TFA salt)	403	С

27	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2. (1-methylpiperidin-2-yl)pyrimidine-	361	D
	N N N N N N N N N N N N N N N N N N N	4-carboxamide (TFA salt)	٠.	
	<b>~</b> сн,			
28	OH OH F	2-[1-(N,N-dimethylglycyl)piperidin- 2-yl]-N-(4-fluorobenzyl)-5,6-	432	I
		dihydroxypyrimidine-4- carboxamide (TFA salt)		
	цс N		-	
29		2-{1-[2-(dimethylamino)-2- oxoethyl]piperidin-2-yl}-N-(4-	432	D
	HC. J.	fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)		
	d,			
30		N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-(1- isonicotinoylpiperidin-2-	494	I
	We a got	yl)pyrimidine-4-carboxamide (TFA salt)	·	
31	OH CYF	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(pyridin-2-ylmethyl)piperidin-2-	438	D
	, , , , , , , , , , , , , , , , , , ,	yl]pyrimidine-4-carboxamide (TFA salt)		
32	N COM	2-(1-benzylpiperidin-2-yl)-N-(2,3- dimethoxybenzyl)-5,6- dihydroxypyrimidine-4-	479	D
		carboxamide (TFA salt)		
	O _			
33	N OH	N-(2,3-dimethoxybenzyl)-2-[1-(N,N)dimethylglycyl)piperidin-2-yl]-5,6-	474	I
		dihydroxypyrimidine-4- carboxamide (TFA salt)	f	
	,			

34 OH OH OH OH	N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-piperidin-2-ylpyrimidine-4-carboxamide	389	A*	
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Table :	18			<u> </u>
1	OH OH	N-benzyl-2-(1-formylpiperidin-3-yl) 5,6-dihydroxypyrimidine-4- carboxamide	357	1
2	OH OH OCH,	N-(2,3-dimethoxybenzyl)-2-(1- formylpiperidin-3-yl)-5,6- dihydroxypyrimidine-4- carboxamide	417	I
3	OH NH NH NH NH NH NH NH NH NH NH NH NH NH	N-(4-fluorobenzyl)-2-(1- formylpiperidin-3-yl)-5,6- dihydroxypyrimidine-4- carboxamide	375	I
4		benzyl 3-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)piperidine-1-carboxylate	481	<b>A</b>
5	OH OH OH OH OH	2-(1-acetylpiperidin-3-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	389	I

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6	ОН	benzyl 3-(4-{[(2-	507	A
-	N OH	ethoxybenzyl)amino]carbonyl}-5,6-	•	
		dihydroxypyrimidin-2-yl)piperidine-		
		1-carboxylate		
	]			
	0 0			
	<b>~</b>			
7	он	benzyl 3-{4-	463	$\mathbf{A}_{\perp}$
	N CONTRACTOR	[(benzylamino)carbonyl]-5,6-		
		dihydroxypyrimidin-2-yl}piperidine-		
	<mark>↓</mark> √	1-carboxylate		
				*.
8	СН	benzyl 3-(4-{[(3-chloro-4-	511	A
	OH NON	methylbenzyl)amino]carbonyl}-5,6-		- <b>-</b> .
i		dihydroxypyrimidin-2-yl)piperidine-		
		1-carboxylate		
-				
		7.45	454	
9	OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	474	I
		[1-(morpholin-4-ylacetyl)piperidin-		
		3-yl]pyrimidine-4-carboxamide		
	À	(TFA salt)		
	<u> </u>			
10	QH	2-(1-benzylpiperidin-3-yl)-N-(4-	437	C
	N OH F	fluorobenzyl)-5,6-		•
		dihydroxypyrimidine-4-	. 1	
	🔰 " 🖁	carboxamide (TFA salt)	İ	1
			. [	
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	-			
11		benzyl 3-(4-{[(2,3-	523	A ·
1	I I I I I	dimethoxybenzyl)amino]carbonyl}-		
		5,6-dihydroxypyrimidin-2-		
l	-''	yl)piperidine-1-carboxylate	٠,	i
	\ \hat{\sigma}			1
ĺ			. ]	
12	~	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	347	A*
12	UT OH	piperidin-3-ylpyrimidine-4-		
į		carboxamide (TFA salt)		
	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \			
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	F	·		
		<u> </u>		

13	OH OH OH F	2-[1-(N,N-dimethylglycyl)piperidin- 3-yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	432	I
14	OH OH	N-benzyl-5,6-dihydroxy-2-piperidin- 3-ylpyrimidine-4-carboxamide (TFA salt)		A*
15	## ## ## ## ## ## ## ## ## ## ## ## ##	N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-piperidin-3-ylpyrimidine-4-carboxamide (TFA salt)	389	A*

Table 1		benzyl 4-(4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)piperidine- l-carboxylate	481	A
2	OH OH N	N-(4-fluorobenzyl)-2-(1- formylpiperidin-4-yl)-5,6- dihydroxypyrimidine-4- carboxamide	375	I
3	ON NO OH OH OH	N-(3,5-dichlorobenzyl)-2-(1- formylpiperidin-4-yl)-5,6- dihydroxypyrimidine-4- carboxamide	425	I

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4	ÓН	benzyl 4-{4-	463	A
	N OH	[(benzylamino)carbonyl]-5,6-	ĺ	
		dihydroxypyrimidin-2-yl}piperidine		1
1		1-carboxylate	ĺ	
			l	ļ
	Ö			i .
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5		benzyl 4-(4-{[(3-chloro-4-	511	
1 3	OH OH OH		711	A
1		methylbenzyl)amino]carbonyl}-5,6-		
		dihydroxypyrimidin-2-yl)piperidine-		
		1-carboxylate .		1
	ö			
6	٣	benzyl 4-(4-{[(2-	507	A
		ethoxybenzyl)amino]carbonyl}-5,6-		
		dihydroxypyrimidin-2-yl)piperidine-	-	
		1-carboxylate		
			•	
7	ОН	benzyl 4-(4-{[(2,3-	523	A
	N OH	dimethoxybenzyl)amino]carbonyl}-		- <b>-</b>
		5,6-dihydroxypyrimidin-2-		
	Lland" & da"	yl)piperidine-1-carboxylate		
	3,	Ar/biberiance-r-carooxyime	· .	
	* 2 · *		- 1	
8		2-[1-(N,N-dimethylglycyl)piperidin-	432	1
	οн		424	*
	N CH CF	4-yl]-N-(4-fluorobenzyl)-5,6-	ł	
		dihydroxypyrimidine-4-		į
	Ma	carboxamide (TFA salt)		
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9	OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	361	С
1	. Joh of	(1-methylpiperidin-4-yl)pyrimidine-	- July 1	~
	N Y N	4-carboxamide (TFA salt)		,
		Teatouxaimue (TFA Sait)	ļ	1
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	що	<b> </b>		
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<u> </u>			<del></del>	
10		N-(4-fluorobenzyl)-5,6-dihydroxy-2-	347	A*
	N OH	piperidin-4-ylpyrimidine-4-	1	[
		carboxamide (TFA salt)	1	. [
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11	OH OH OH, OH,	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-piperidin-4- ylpyrimidine-4-carboxamide (TFA salt)	389	A*
12	£ \$ \$ \$	N-benzyl-5,6-dihydroxy-2-piperidin- 4-ylpyrimidine-4-carboxamide (TFA salt)	329	A*

Table	Table 20					
1	ÖH ÖH N	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (1,2,3,4-tetrahydroquinolin-2- yl)pyrimidine-4-carboxamide (TFA salt)	395	A*		
2		benzyl 2-(4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)-3,4- dihydroquinoline-1(2H)-carboxylate	529	A		
3	0H 2	2-(1-benzoyl-1,2,3,4- tetrahydroquinolin-2-yl)-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	499	I		
4	OH OH OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (1-methyl-1,2,3,4- tetrahydroquinolin-2-yl)pyrimidine- 4-carboxamide (TFA salt)	409	С		

5	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-(pyridin-2-ylcarbonyl)-1,2,3,4- tetrahydroquinolin-2-yl]pyrimidine- 4-carboxamide (TFA salt)	500	I
6	2-(1-benzyl-1,2,3,4- tetrahydroquinolin-2-yl)-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	485	С

Tabl	le 21			
1		2-(1-benzoylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)	452	A*
2	H,C ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) (	2-[1-(2-chlorobenzoyl)-4- methylpiperazin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (HCl salt)	500	I
3	CH, NOH OH NOH NOH NOH NOH NOH NOH NOH NOH	2-(4-acetyl-1-methylpiperazin-2-yl)- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	404	I
4	OH OH OH	2-(4-benzoyl-1-methylpiperazin-2- yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	466	I
5	H,C, N, N, O, N, N, N, N, N, N, N, N, N, N, N, N, N,	2-[1-(4-chlorobenzoyl)-4- methylpiperazin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	500	I

6	CH, OH OH	2-{4-[(ethylamino)carbonyl]-1- methylpiperazin-2-yl}-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	433	G
7	H ₂ C _N H ₃ C _N H ₄ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅ C _N H ₅	2-[1-(3-chlorobenzoyl)-4- methylpiperazin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	500	I
8	CH ₃ OH OH F	2-(4-ethyl-1-methylpiperazin-2-yl)- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	390	C
9	H,C N N OH	2-(1-benzoyl-4-ethylpiperazin-2-yl)- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	480	С
10	CHO N OH, N OH,	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-methyl-4- (methylsulfonyl)piperazin-2- yl]pyrimidine-4-carboxamide (TFA salt)	440	I
11	#c///	2-(1-benzoyl-4-methylpiperazin-2- yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	466	Ī
12	OH OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (1-methylpiperazin-2-yl)pyrimidine- 4-carboxamide (TFA salt)		A*

13	<b>р</b> н	tert-butyl 3-(4-{[(4-	462	C
	Jun St. 8	fluorobenzyl)amino]carbonyl}-5,6-	İ	1
		dihydroxypyrimidin-2-yl)-4-		
		methylpiperazine-1-carboxylate		1
	~ oi,	(TFA salt)	1	
		·	l	1
1			. *	
14	ОН	2-(1,4-dimethylpiperazin-2-yl)-N-(4-	27/	<del> </del>
1	J 4	2-(1,4-dimetry)piperazin-2-yi)-in-(4-	376	C
	N N	fluorobenzyl)-5,6-		1
1	HC N	dihydroxypyrimidine-4-	,	1
		carboxamide (TFA salt)		
1	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\			
1			•	l .
			<u> </u>	
15	ÓН	tert-butyl 3-(4-{[(4-	448	A*
1	ON ON ON ON	fluorobenzyl)amino]carbonyl}-5,6-		1
1		dihydroxypyrimidin-2-yl)piperazine-		
1		1-carboxylate (TFA salt)		1
1				
1				
16	. QH	2-[1-benzoyl-4-(N,N-	537	<del></del>
		dimethylglycyl)piperazin-2-yl]-N-(4	331	I
1.		fluorobenzyl)-5,6-		
ļ				
		dihydroxypyrimidine-4-		
		carboxamide (TFA salt)		
17				
17	(♠ o#	2-(4-benzyl-1-methylpiperazin-2-yl)	452	, <b>C</b>
	OH OF	N-(4-fluorobenzyl)-5,6-		
1 1		dihydroxypyrimidine-4-		
		carboxamide (TFA salt)		1
	/ Viva ö			ı
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لــــــا				
18	он	2-(1-benzoyl-4-isopropylpiperazin-2	494	С
	OH NOTE	yl)-N-(4-fluorobenzyl)-5,6-		_
		dihydroxypyrimidine-4-		1
		carboxamide (TFA salt)	. [	
	~ ~	(as to state)		ł
			. 1	
			1	J
19	. OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	404	С
	JOH A F	(1-isopropyl-4-methylpiperazin-2-	+0+	١ ٦
			1	
- 1	H _C N N N	yl)pyrimidine-4-carboxamide (TFA	- 1	ļ
	L N COL O	asit)	ı	ļ
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			,	
20	OH OH OF	benzyl 2-(4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)piperazine- 1-carboxylate (TFA salt)	482	A*
21	O 9 ⁴	2-[4-(anilinocarbonyl)-1-	481	G
	OT WORLD	methylpiperazin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)		
22		1-benzyl 4-tert-butyl 2-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)piperazine-1,4-dicarboxylate	580 (M-)	A
23	HC C C C C C C C C C C C C C C C C C C	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [4-methyl-1-(pyridin-2- ylcarbonyl)piperazin-2- yl]pyrimidine-4-carboxamide (TFA salt)	467	С
24	OH OH OH OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [1-methyl-4-(pyridin-2- ylcarbonyl)piperazin-2- yl]pyrimidine-4-carboxamide (TFA salt)	467	Ĭ
25	H ₂ C N N OH N F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (4-isopropyl-1-methylpiperazin-2- yl)pyrimidine-4-carboxamide (TFA salt)	404	С
26	H ₃ C N O O O O CH ₃ CH ₃	2-[1-(N,N-dimethylglycyl)-4- methylpiperazin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	447	I

27	OH OH N P F	2-[1-(N,N-dimethylglycyl)piperazin- 2-yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	433	A*
28	CHON, NO CH, CH, CH, CH, CH, CH, CH, CH, CH, CH,	tert-butyl 4-(N,N-dimethylglycyl)-3- (4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)piperazine- 1-carboxylate (TFA salt)	533	I
29	H _C C N N N N N N N N N N N N N N N N N N	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (4-methylpiperazin-2-yl)pyrimidine- 4-carboxamide (TFA salt)	362	A*
30	OH N N N N N N N N N N N N N N N N N N N	N-(4-fluorobenzyl)-5,6-dihydroxy-2- piperazin-2-ylpyrimidine-4- carboxamide (TFA salt)	348	A*

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Table 1	e 22	N-(4-fluorobenzyl)-5,6-dihydroxy-2 (4-methylmorpholin-3- yl)pyrimidine-4-carboxamide (TFA salt)	363	C
2	OH OH	2-(4-benzyl-5-oxomorpholin-3-yl)- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	453	A
3	OH OH OH	2-(4-benzylmorpholin-3-yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	439	C
4	OH OH N	N-(4-fluorobenzyl)-5,6-dihydroxy-2- morpholin-3-ylpyrimidine-4- carboxamide (TFA salt)	349	A*

Table	e 23			
1	O-O-C-O-C-O-C-O-C-O-C-O-C-O-C-O-C-O-C-O	2-[(2S,4R)-4-(benzyloxy)-1- methylpyrrolidin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	453	A
2	HO Chirat	2-[(2S,4R)-1-benzoyl-4- hydroxypyrrolidin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	453	

				*
3	ÇH Chirel	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	363	A*
1	OH OF	[(2S,4R)-4-hydroxy-1-		
		methylpyrrolidin-2-yl]pyrimidine-4-	٠.	l
	HO	carboxamide (TFA salt)		
	`CH,			
4	OH Chiral	2-[(2S,4R)-1-benzyl-4-	529	С
1		(benzyloxy)pyrrolidin-2-yl]-N-(4-		
		fluorobenzyl)-5,6-		
	ا سر	dihydroxypyrimidine-4-		
		carboxamide		
İ		·		]
5	OH	2-(1-benzoylpyrrolidin-2-yl)-N-(4-	437	1
1		fluorobenzyl)-5,6-		
		dihydroxypyrimidine-4-		
٠.	-N-0 0	carboxamide	İ	
l				-
<u> </u>				
6	OH CL	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	467	A
		[1-(4-methoxybenzyl)-5-		
		oxopyrrolidin-2-yl]pyrimidine-4-		
l	\rangle \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \cdot\ \	carboxamide		
<b>.</b>	l° d			
	4			
	, a,			
7	OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	333	A*
	↓ OH	pyrrolidin-2-ylpyrimidine-4-		Ī
		carboxamide (TFA salt)	ı	
				1
	\ \n\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \			. [
				- 1
8	он chied	2-{(2S,4R)-4-(benzyloxy)-1-(N,N-	524	I
		dimethylglycyl)pyrrolidin-2-yl]-N-	-	]
		(4-fluorobenzyl)-5,6-	İ	1
		dihydroxypyrimidine-4-	į	[
j	, hor	carboxamide (TFA salt)	l	İ
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9		N (4 fluorohanzul) 5 6 dibuda 2	347	D
"	OH .	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	34/	ע
1	N OH F	(1-methylpyrrolidin-2-yl)pyrimidine	1	
		4-carboxamide (TFA salt)	I	'
	(		.	
	V_N, Ö CH,	. I	1	İ
	<b>₩</b> 3	· [	]	.

		1	540	
10	OH OH CHICAL	2-[(2S,4R)-1-benzoyl-4- (benzyloxy)pyrrolidin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	543	I
11	OH OH OH	2-(1-benzylpyrrolidin-2-yl)-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	423	D
12	CH CH CH CH CH CH CH CH CH CH CH CH CH C	2-(1-benzoylpyrrolidin-2-yl)-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	479	I
13	HO	tert-butyl (2S,4R)-2-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-4-hydroxypyrrolidine-1-carboxylate	449	A*
14	OH OH Ohral	2-{(2S,4R)-4-(benzyloxy)-1-[4- (diethylamino)benzoyl]pyrrolidin-2- yl}-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	614	I
15	HO N	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [(2S,4R)-4-hydroxypyrrolidin-2- yl]pyrimidine-4-carboxamide (TFA salt)	349	A*
16	OH OH OH F	2-[1-(N,N-dimethylglycyl)pyrrolidin 2-yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (TFA salt)	418	I

17	OH OH OH OH OH OH OH OH OH OH OH OH OH O	2-{1-[2-(dimethylamino)-2-oxoethyl]pyrrolidin-2-yl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide (TFA salt)	418	D
18	Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Chiral Ch	tert-butyl (2S,4R)-4-(benzyloxy)-2- (4-{[(4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)pyrrolidine 1-carboxylate	539	A
19	Chiest	2-[(2S,4R)-4-(benzyloxy)pyrrolidin- 2-yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide (HCl salt)	439	A*

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Table	e 24
1	

		N-(1,1'-biphenyl-3-ylmethyl)-5,6- dihydroxy-2-pyridin-2-ylpyrimidine 4-carboxamide (HCl salt)	399	A
2	OH OH OH	N-(3-chloro-4-fluorobenzyl)-5,6- dihydroxy-2-pyridin-2-ylpyrimidine- 4-carboxamide (HCl salt)	375	A
3	OH OH PF	N-(4-fluorobenzyl)-5,6-dihydroxy-2- pyridin-2-ylpyrimidine-4- carboxamide (HCl salt)	341	A
4	OH OH OH	N-(3-chlorobenzyl)-5,6-dihydroxy-2 pyridin-2-ylpyrimidine-4- carboxamide (HCl salt)	357	<b>A</b>

5	OH OH CH,	N-(3-chloro-4-methylbenzyl)-5,6- dihydroxy-2-pyridin-2-ylpyrimidine- 4-carboxamide (HCl salt)	371	A
6	OH OH OH, OCH,	N-(2,3-dimethoxybenzyl)-5,6- dihydroxy-2-pyridin-2-ylpyrimidine- 4-carboxamide (HCl salt)	383	A
7	OH OH CH,	N-(2,3-dimethylbenzyl)-5,6- dihydroxy-2-pyridin-2-ylpyrimidine- 4-carboxamide (HCl salt)	351	A
8	OH OH OH OH	N-(2-chloro-4-fluorobenzyl)-5,6- dihydroxy-2-pyridin-2-ylpyrimidine- 4-carboxamide (HCl salt)	375	A
9	OH OH H ₃ C	5,6-dihydroxy-N-(2-methoxybenzyl) 2-pyridin-2-ylpyrimidine-4- carboxamide (HCl salt)	353	A
10	OH OH	N-benzyl-5,6-dihydroxy-2-pyridin-2 ylpyrimidine-4-carboxamide (HCl salt)	323	A
11	OH OH OH	5,6-dihydroxy-2-pyridin-2-yl-N- (pyridin-3-ylmethyl)pyrimidine-4- carboxamide (TFA salt)	324	A

12 OH OH OH Carboxamide (TF	hyl)pyrimidine-4-	A
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Table 15B	<del></del>	3.0	
Strucuture	name	M+1	Procedure
OH OH CH ₃ CH ₃ CH ₃	benzyl 1-[4-({[4-fluoro-2- (methylsulfonyl)benzyl]amino}carbony l)-5,6-dihydroxypyrimidin-2-yl]-1- methylethylcarbamate		A
H ₂ N OH H H ₃ C CH ₃ O O=S=O CH ₃	2-(1-amino-1-methylethyl)-N-[4-fluoro- 2-(methylsulfonyl)benzyl]-5,6- dihydroxypyrimidine-4-carboxamide	399	A*
CH ₃ N OH OH OH OH OH OH OH OH OH OH OH OH OH	2-[1-(dimethylamino)-1-methylethyl]-N [4-fluoro-2-(methylsulfonyl)benzyl]-5,6 dihydroxypyrimidine-4-carboxamide		С
NH2 NH2 PF	2-(1-aminocyclopropyl)-N-(4- fluorobenzyl)-5,6-dihydroxypyrimidine- 4-carboxamide	319	A*
CH3 N OH OH	2-[1-(dimethylamino)cyclopropyl]-N-(4 fluorobenzyl)-5,6-dihydroxypyrimidine- 4-carboxamide	347	С
CN N OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1- [(pyrazin-2- ylcarbonyl)amino]cyclopropyl]pyrimidi ne-4-carboxamide	425	
OH OH OH	benzyl 1-(4-[[(4- fluorobenzyl)amino]carbonyl]-5,6- dihydroxypyrimidin-2- yl)cyclopentylcarbamate	481	A
NH ₂ OH F	2-(1-aminocyclopentyl)-N-(4- fluorobenzyl)-5,6-dihydroxypyrimidine- 4-carboxamide		A*
CH ₃ N OH OH F	2-[1-(dimethylamino)cyclopentyl]-N-(4- fluorobenzyl)-5,6-dihydroxypyrimidine- 4-carboxamide	375	С

			<del></del>
ОН	2-(1-{[(ethylamino)carbonyi]amino}-1-	392	G
J OH ∠ F	methylethyl)-N-(4-fluorobenzyl)-5,6-	1	
CHO H H N H	dihydroxypyrimidine-4-carboxamide	ſ	1
	<b>   </b>	ł ·	1 .
II ~ A X M A ~ ~	•	1	· ·
Ö CH3CH3 Ö	11	1	ļ ·
	<u> </u>	<u></u>	J
ļ ŅН	2-[1-(benzylamino)-1-methylethyl]-N-	411	C
OH OF	(4-fluorobenzyl)-5,6-		1.
	dihydroxypyrimidine-4-carboxamide	l .	,
		1	1 .
, н _я с́он, ö		]	
		l	l .
		<u> </u>	
OH	2-[1-(benzoylamino)-1-methylethyl]-N-	425	1
OH OF	(4-fluorobenzyl)-5,6-	i	
	dihydroxypyrimidine-4-carboxamide		
H,C CH,	:	1	
0 H3C CM3 O		j	
		l i	
	0 (4 (harmattan)	<u> </u>	
ρн	2-(1-[benzyl(methyl)amino]-1-	425	С
CH N OH OF	methylethyl]-N-(4-fluorobenzyl)-5,6-		
	dihydroxypyrimidine-4-carboxamide		
HC CH	1		٠.
G € ~ 50			
		•	
OH.	2-[1-(dimethylamino)-1-methylethyl]-N	275	· ·
OH ~	(2-ethoxybenzyl)-5,6-	375	Α
CH N OH	dihydroxypyrimidine-4-carboxamide	1	* • •
	di iydioxypyrimidine-4-carboxamide	- 1	
LP HC CH I			
13-5-3		. 1	
ĊH ₃			
ОН	N-(2-chlorobenzyi)-2-[1-	365	Α
· · · · · · · · · · · · · · · · · · ·	(dimethylamino)-1-methylethyl]-5,6-	000	. ^
CH³ N OH	dihydroxypyrimidine-4-carboxamide	- 1	
Ki la 4 ki la 4	danyoroxypyranidine 4 danboxaniide	- 1	
H³C, N N N	,	- 1	
ัน _ร ี่CH ₃ Ö cٰl		. [	
ОН	N-(2-chlorobenzyl)-2-[1-	383	. A
	(dimethylamino)-1-methylethyl]-5,6-	í	,
CH N	dihydroxypyrimidine-4-carboxamide		
		1	
H ³ C, N		. 1	f
Ling City City	[		
ÓН	N-(5-chloro-2-methylbenzyl)-2-[1-	379	Α
OHH ₃ C	(dimethylamino)-1-methylethyl]-5,6-	- 1	
CH ³ N H H	dihydroxypyrimidine-4-carboxamide	- 1	
H,C'N N N CI		- 1	
"H,C CH,"		- 1	
33 0	1	- 1	
ОН	NI (A fluorabassal) E 2 db d	1=-	
	N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-	427	
N N NOH NF	methyl-1-[(pyrazin-2-	1	[
	ylcarbonyl)amino]ethyl}pyrimidine-4-	- 1	
" "HCCH" [	carboxamide	1	- 1
0.3- 0.3	. [	- 1	]
	I		.

			<del>- ,</del>
H ₃ C CH ₃ OH F	2-[1-(diethylamino)-1-methylethyl]-N- (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	377	К
OH OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1- methyl-1-morpholin-4- ylethyl)pyrimidine-4-carboxamide	391	K
OH OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1- methyl-1-piperidin-1- ylethyl)pyrimidine-4-carboxamide	389	ĸ
OH OH H ₃ C CH ₃ O	N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1- methyl-1-pyrrolidin-1- ylethyl)pyrimidine-4-carboxamide	375	К
OH OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1- methyl-1-{methyl(pyridin-4- ylmethyl)amino]ethyl)pyrimidine-4- carboxamide	426	C
CH ₃ N OH S _{CH₃}	2-[1-(dimethylamino)-1-methylethyl]- 5,6-dihydroxy-N-[2- (methylthio)benzyl]pyrimidine-4- carboxamide	377	A
OH OH H N N N N N N N N N N N N N N N N	N1,N1-diethyl-N2-[1-(4-[[4- fluorobenzyl)amino]carbonyl}-5,6- dihydroxypyrimidin-2-yl)-1- methylethyl]ethanediamide	448	
OH OH H	2-[1-(1,4-dioxa-8-azaspiro[4.5]dec-8- yl)-1-methylethyl]-N-(4-fluorobenzyl)- 5,6-dihydroxypyrimidine-4- carboxamide	447	К
OH OH OH CH ₃ CH ₃ CH ₃ CH ₃	N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1- methyl-1-{{(1-methyl-1H-imidazol-2- yl)carbonyl]amino}ethyl)pyrimidine-4- carboxamide	429	

N-(4-fluorobenzy)-5,6-dihydroxy-2-{1-   403   K   methyl-1-(4-oxop)peridin-1-1   yl)ethyl pyrimidine-4-carboxamide   N-(4-fluorobenzy)-5,6-dihydroxy-2-{1-   426   C   methyl-1-(methyl-1-(4-fluorobenzy)-5,6-dihydroxy-2-{1-   426   C   methyl-1-(methyl-1-2-yl)-1   methylethyl-4-methylmorpholine-2-carboxamide   N-(1-(4-fluorobenzy))-5,6-dihydroxypyrimidin-2-yl)-1   methylethyl-4-methylmorpholine-2-carboxamide   N-(2-(1-(acetylamino)-1-methylethyl)-N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(2-(1-(acetylamino)-1-methylethyl)-N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(2-(1-(dimethylamino)-1-methylethyl)-N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(2-(1-(dimethylamino)-1-methylethyl)-N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(2-(1-(dimethylamino)-1-methylethyl)-N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(2-(1-(dimethylamino)-1-methylethyl)-N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(2-(1-(dimethylamino)-1-methylethyl)-N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(4-fluorobenzy))-5,6-dihydroxypyrimidine-4-carboxamide   N-(4-fluorobenzy)-5,6-dihydroxypyrimidine-4-carboxamide   N-(4-fluorobenzy)-5,6-dihydroxypyrimidine-4-carboxamide   N-(4-flu				
methyl-1-[methyl(pyridin-2-ylynethyl)amino]ethyl)pyrimidine-4-carboxamide  CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₃ OH OH CH ₄ OH CH ₃ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₄ OH CH ₅ OH CH ₄ OH CH ₄ OH CH ₅ OH CH ₅ OH CH ₅ OH CH ₆ OH CH ₅ OH CH ₆ OH CH ₆ OH CH ₆ OH CH ₇ OH CH ₆ OH CH ₇ OH CH ₇ OH CH ₈ OH CH ₈ OH CH ₈ OH CH ₈ OH CH ₈ OH CH ₉ OH CH ₈ OH CH ₉ OH CH ₈ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH CH ₉ OH		methyl-1-(4-oxopiperidin-1-	1- 403	К
fluorobenzyl)amino carbonyl]-5,6-dihydroxypyrimidin-2-yl)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide    CH ₃ N	Ch ch, n oh	methyl-1-[methyl(pyridin-2- ylmethyl)amino]ethyl)pyrimidine-4-	426	C
H ₃ C H ₃ N H H H H H H H H H H H H H H H H H H	OH OH OH	fluorobenzyl)amino]carbonyl]-5,6- dihydroxypyrimidin-2-yl]-1- methylethyl]-4-methylmorpholine-2-	448	1
H ₃ C H ₃ CH ₃ OH H ₄ CH ₃ CH ₃ OH OH H ₄ CH ₃ CH ₃ OH OH H ₄ CH ₃ CH ₃ OH OH H ₄ CH ₃ CH ₃ OH OH H ₄ CH ₃ CH ₃ OH OH OH H ₄ CH ₃ CH ₃ OH OH OH OH OH OH OH OH OH OH OH OH OH	•	methylethyl)-N-(4-fluorobenzyl)-5,6-	377	1
H ₃ C CH ₃ OH  OH  CH ₃ N-(2,3-dimethoxybenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide  N-(2,3-dimethoxybenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide  OH  CH ₃ N-(H ₃ C)  OH  CH ₃ N-(H ₃ C)  OH  OH  OH  N-(4-fluorobenzyl)-5,6-dihydroxy-2-(7-arethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide  N-(4-fluorobenzyl)-5,6-dihydroxy-2-(7-arethyl-1-yl)pyrimidine-4-carboxamide	H ₃ C N N N N N N N N N N N N N N N N N N N	(4-fluorobenzyl)-5,6-	363	
CH ₃ N-(4-fluorobenzyl)-5,6-dihydroxy-2-(7-methyl-7-azabicyclo[2.2.1]hept-1-yl)pyrimidine-4-carboxamide	H ₃ C CH ₃ OH OH F	1-methylethyl}-N-(4-fluorobenzyl)-5.6-		E
OH OH OH OH OH OH OH OH OH OH OH OH OH O	H _C CH, N OH OCH,	(dimethylamino)-1-methylethyl]-5,6-	391	A
methyl-7-azabicyclo[2.2.1]hept-1-yl)pyrtmidine-4-carboxamide	ع د ۱	pyran-4-yi]-N-(4-fluorobenzyl)-5,6-		С
	N N OH F	methyl-7-azabicyclo[2.2,1]hept-1-	373	С

OH OH OH OH OH OH OH OH OH OH OH OH OH O	2-(7-acetyl-7-azabicyclo[2.2.1]hept-1- yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	401	A
OH OH H	2-(2-acetyl-2-azabicyclo[2.1.1]hex-1- yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	387	A
OH OH H N N N N N N N N N N N N N N N N	N-(4-fluorobenzyl)-5,6-dihydroxy-2-(2- methyl-2-azabicyclo[2.1.1]hex-1- yl)pyrimidine-4-carboxamide	359	С

Table 17B			
Structure	Name	M+1	Procedure
CH, CH,	tert-butyl (2S,4R)-4-(benzyloxy)-2-(4 {[(4-fluorobenzyl)amino]carbonyl}- 5,6-dihydroxypyrimidin-2- yl)piperidine-1-carboxylate	553	A
OH OH OH OH	2-[(2S,4R)-4-(benzyloxy)piperidin-2- yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	453	A*
OH OH OH	2-[(2S,4R)-4-(benzyloxy)-1- methylpiperidin-2-yl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	467	С
HO NOH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [(2S,4R)-4-hydroxy-1- methylpiperidin-2-yl]pyrimidine-4- carboxamide	377	A*
OH OH OH OH OH OH OH OH OH OH OH OH OH O	2-[1-acetyl-4-(benzyloxy)piperidin-2- yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	495	

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Structure	Name	M+1	Procedure
H,C,N,N,O,D,F	2-(1-ethyl-4-methylpiperazin-2-yl)-N- (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	390	A
H,C. N, NO OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2-[4-methyl-1-(pyrazin-2-ylcarbonyl)piperazin-2-yl]pyrimidine-4-carboxamide		A

Table 22B			
Structure	Name		Procedure
OH N OH N O CH, H,C CH,	tert-butyl 3-(4-{[(4- fluorobenzyl)amino]carbonyl}- 5,6-dihydroxypyrimidin-2- yl)thiomorpholine-4-carboxylate	465	А
S NH OH	N-(4-fluorobenzyl)-5,6- dihydroxy-2-thiomorpholin-3- ylpyrimidine-4-carboxamide	365	A*
S-N-CH3	N-(4-fluorobenzyl)-5,6- dihydroxy-2-(4- methylthiomorpholin-3- yl)pyrimidine-4-carboxamide	379	С
SHOP OH OH	N-(4-fluorobenzyl)-5,6- dihydroxy-2-[4-(pyridin-2- ylcarbonyl)thiomorpholin-3- yl]pyrimidine-4-carboxamide	470	<b>i</b>
S CH ₃	2-(4-acetylthiomorpholin-3-yl)- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	407	ı
H ₃ C O H ₃ H _N C CH ₃	tert-butyl 1-(4-{[(4- fluorobenzyl)amino]carbonyl}- 5,6-dihydroxypyrimidin-2-yl)-2- methoxyethylcarbamate	437	A

H ₃ C. OH OH HN OH HN F	2-[1-(dimethylamino)-2- methoxyethyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	365	С
H ₃ C ₁ OH OH HN OH	2-[1-(acetylamino)-2- methoxyethyl]-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	379	
H ₃ C _{.O} NH ₂ HN	2-(1-amino-2-methoxyethyl)-N- (4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	337	A*
OH OH OH OH OH OH OH OH OH OH	N-(4-fluorobenzyl)-5,6- dihydroxy-2-{2-methoxy-1- [(pyridin-2- ylcarbonyl)amino]ethyl}pyrimidi ne-4-carboxamide	442	
H ₂ C-O+NOH H	N-(4-fluorobenzyl)-2-[1- (formylamino)-2-methoxyethyl]- 5,6-dihydroxypyrimidine-4- carboxamide		A

H ₃ C-O-NH OH H ₃ C-NH O	N-(4-fluorobenzyl)-5,6- dihydroxy-2-[2-methoxy-1- (methylamino)ethyl]pyrimidine- 4-carboxamide	352	A
H ₂ C-0 CH ₃ O	2-{1-[acetyl(methyl)amino]-2- methoxyethyl}-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	393	
H _C C _{H,C} C N	N-(4-fluorobenzyl)-5,6- dihydroxy-2-{2-methoxy-1- [methyl(pyridin-2- ylcarbonyl)amino]ethyl}pyrimidi ne-4-carboxamide	456	•

Table 23B			5
Structure	Name	M+1	Procedure
OH OH F	N-(4-fluorobenzyl)-5,6- dihydroxy-2-[(4R)-3- (pyridin-2-ylcarbonyl)-1,3- thiazolidin-4-yl]pyrimidine-4 carboxamide		
		456	
S NH OH F	N-(4-fluorobenzyl)-5,6- dihydroxy-2-[(4R)-1,3- thiazolidin-4-yl]pyrimidine-4 carboxamide		
,		351	A*
S—N—OH—OH—F	N-(4-fluorobenzyl)-5,6- dihydroxy-2-[(4R)-3-methyl- 1,3-thiazolidin-4- yl]pyrimidine-4- carboxamide	365	С
	O (0		<del>                                     </del>
OH OH H	2-(3-acetyl-1,3-thiazolidin-2 yl)-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4- carboxamide	·	
3		393	1
SHOH OH OH CH3	N-(4-fluorobenzyl)-5,6- dihydroxy-2-(3-methyl-1,3- thiazolidin-2-yl)pyrimidine- 4-carboxamide		
		365	C

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Table 25B		_	
Structure	Name	M+1	Procedure
	N-(4-fluorobenzyl)-5,6-dihydroxy-2-	390	C
ОН	(1,2,4-trimethylpiperazin-2-		}
N OH	yl)pyrimidine-4-carboxamide	İ	
		}	
		1	1
N CH ₃ O		'	
·			· .
ОН	2-[2,4-dimethyl-1-(pyrazin-2-	482	С
l	ylcarbonyl)piperazin-2-yl]-N-(4-		
ICH CHI I I	fluorobenzyl)-5,6-	ŀ	
	dihydroxypyrimidine-4-carboxamide		
	2-(1-acetyl-2,4-dimethylpiperazin-2-	418	. C
ОН	yl)-N-(4-fluorobenzyl)-5,6-		
OH OH	dihydroxypyrimidine-4-carboxamide		
ICH NO NO NO NO NO NO NO NO NO NO NO NO NO			
			* .
Сн			. •
он	tert-butyl 1-(4-{[(4-	451	, A
N OH OF	fluorobenzyl)amino]carbonyl}-5,6-		
HC-0HS-LLLL	dihydroxypyrimidin-2-yl)-2-methoxy-		
I, o L w H o	1-methylethylcarbamate		
I ON O		1	
H ₂ C_CO			
CH.			
3	·		
ÓН	2-(1-amino-2-methoxy-1-	351	Α*
OH F	methylethyl)-N-(4-fluorobenzyl)-5,6-	1	
LHC-H9 L L L L L	dihydroxypyrimidine-4-carboxamide		· .
1.3~2. 1. N. J., ~ ~ ~			
NH ₂ Ö			
			1
	·		
<b>ОН</b>	2-[1-(acetylamino)-2-methoxy-1-	393	
NOH OF	methylethyl]-N-(4-fluorobenzyl)-5,6-		
H3C-0-H3C	dihydroxypyrimidine-4-carboxamide		
HN O O	· .	İ	
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сн,	,	•	
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H ₃ C-O-N-CH ₃ OH	2-[1-(dimethylamino)-2-methoxy-1-methylethyi]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	379	С
H ₃ C-NH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [2-methoxy-1-methyl-1- (methylamino)ethyl]pyrimidine-4- carboxamide	365	C .
H ₃ C-OHC N H F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- (2-methoxy-1-methyl-1-[(pyridin-2- ylcarbonyl)amino]ethyl]pyrimidine-4- carboxamide	456	G
CH ₃ OH H F	2-(1,2-dimethylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide	375	С
H ₃ C-OHOH H H ₃ C-NOO O	2-{1-[acetyl(methyl)amino]-2- methoxy-1-methylethyl}-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	407	1
H ₃ C ₀ H ₄ C _N NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	N-(4-fluorobenzyl)-5,6-dihydroxy-2- {2-methoxy-1-methyl-1- [methyl(pyridin-2- ylcarbonyl)amino]ethyl)pyrimidine-4- carboxamide	470	
H,C-0-H,C-H, OH	2-{1- [(cyclohexylmethyl)(methyl)amino]- 2-methoxy-1-methylethyl}-N-(4- fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	461	С

		·	
H ₂ C- ₀ H ₂ C N OH F	2-{1-[(cyclohexylmethyl)amino]-2- methoxy-1-methylethyl}-N-(4- fluorobenzyl)-5,6-	447	С
NH "	dihydroxypyrimidine-4-carboxamide	·	
OH OH F	2-{1-[(cyclohexylmethyl)amino]-2-methoxy-1-methylethyl}-N-(4-	361	A*
HCINH	fluorobenzyi)-5,6- dihydroxypyrimidine-4-carboxamide	·	
<b>~</b>			·
<b>О</b> Н	2-(4-acetyl-1,2-dimethylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-	418	Α
CH, N OH	dihydroxypyrimidine-4-carboxamide		-
OH OH F	2-(1-acetyl-2-methylpiperidin-2-yl)- N-(4-fluorobenzyl)-5,6-	403	Α
CHI N	dihydroxypyrimidine-4-carboxamide		
CH ₃			
OH OH	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [2-methyl-1-(pyrazin-2-	467	. <b>A</b>
H.C. N.	ylcarbonyl)piperidin-2-yl]pyrimidine- 4-carboxamide		
N Z			
OH OH	N-(2,3-dimethoxybenzyl)-2-(1,2-dimethylpiperidin-2-yl)-5,6-	417	С
HC N OMe	dihydroxypyrimidine-4-carboxamide		
<b>С</b> н,			
OH OH F	N-(4-fluorobenzyl)-5,6-dihydroxy-2- [2-methyl-1-(pyridin-2-	466	A
	ylcarbonyl)piperidin-2-yl]pyrimidine- 4-carboxamide		
<del></del>	<u> </u>		

CH ₃ CH ₄ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅	2-{1-[(2,4-dimethyl-1,3-thiazol-5- yl)carbonyl]-2-methylpiperidin-2-yl}- N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	500	А
OH OH H N CH ₉ O CH ₉	2-[(2S)-1-acetyl-2-methylpyrrolidin- 2-yl]-N-(4-fluorobenzyl)-5,6- dihydroxypyrimidine-4-carboxamide	389	A

While the foregoing specification teaches the principles of the present invention, with examples provided for the purpose of illustration, the practice of the invention encompasses all of the usual variations, adaptations and/or modifications that come within the scope of the following claims.

#### WHAT IS CLAIMED IS:

### 1. A compound of Formula (I):

#### 5 wherein

R¹ is

(1) -H,

(2) -C₁₋₆ alkyl, which is optionally substituted with one or more substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-C₀₋₆ alkyl-N(RaRb), N(Ra)-C(=O)-C₀₋₆ alkyl-N(RbRc), -SO₂Ra, -N(Ra)SO₂Rb, -SO₂N(RaRb),

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 $-N(R^a)C(=O)C(=O)N(R^bR^c)$ , or  $-N(R^a)C(=O)OR^b$ ,

(3) -O-C₁₋₆ alkyl, which is optionally substituted with one or more substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-C₀₋₆ alkyl-N(RaRb), N(Ra)-C(=O)-C₀₋₆ alkyl-N(RbRc), -SO₂Ra, -N(Ra)SO₂Rb, -SO₂N(RaRb), or -N(Ra)-C(Rb)=O,

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- $(4) -R^{k},$
- -C₁₋₆ alkyl-R^k, wherein the alkyl is optionally substituted with one or more substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -N(R^aR^b), -N(R^a)CO₂R^b, -N(R^a)C(=O)-C₀₋₆ alkyl-N(R^bR^c), or -N(R^a)-C₂₋₆ alkyl-OH with the proviso that the -OH is not attached to the carbon alpha to N(R^a),

:	(6)	-C2-5 alkenyl-Rk,
•	(7)	-C2-5 alkynyl-Rk,
	(8)	-C ₀₋₆ alkyl-O-C ₀₋₆ alkyl-R ^k ,
	(9)	$-C_{0-6}$ alkyl- $S(O)_n$ - $C_{0-6}$ alkyl- $R^k$ ,
5	(10)	-O-C ₁₋₆ alkyl-OR ^k ,
	(11)	-O-C ₁₋₆ alkyl-O-C ₁₋₆ alkyl-R ^k ,
	(12)	-O- $C_{1-6}$ alkyl- $S(O)_n R^k$ ,
•	(13)	-C ₀₋₆ alkyl-N(Ra)-Rk,
	(14)	-C ₀₋₆ alkyl-N(R ^a )-C ₁₋₆ alkyl-R ^k ,
10	(15)	-C ₀₋₆ alkyl-N(R ^a )-C ₁₋₆ alkyl-OR ^k ,
	(16)	$-C_{0-6}$ alkyl-C(=O)-R ^k ,
	(17)	-C ₀₋₆ alkyl-C(=O)N( $R^a$ )-C ₀₋₆ alkyl- $R^k$ ,
. ·	(18)	- $C_{0-6}$ alkyl- $N(R^a)C(=0)$ - $C_{0-6}$ alkyl- $R^k$ ,
	(19)	$-C_{0-6}$ alkyl-N(Ra)C(=O)-O-C ₀₋₆ alkyl-R ^k ,
15	(20)	-C ₁₋₆ alkyl which is:
		(i) substituted with aryl or -O-aryl, wherein the aryl is optionally
		substituted with one or more substituents each of which is
	•	independently halogen, -OH, -C ₁₋₆ alkyl, -C ₁₋₆ alkyl-ORa,
		-C ₁₋₆ haloalkyl, -O-C ₁₋₆ alkyl, -O-C ₁₋₆ haloalkyl,
20		methylenedioxy attached to two adjacent carbon atoms, or aryl;
		(ii) substituted with $-R^k$ , $-C_{1-6}$ alkyl- $R^k$ , $-N(R^a)$ - $C(=0)$ - $C_{0-6}$
		alkyl- $\mathbb{R}^k$ , -C ₀₋₆ alkyl-N( $\mathbb{R}^a$ )-C ₀₋₆ alkyl- $\mathbb{R}^k$ , -C ₀₋₆
		alkyl-O-C ₀₋₆ alkyl- $\mathbb{R}^k$ , or -C ₀₋₆ alkyl-N( $\mathbb{R}^a$ )-C(=O)-C ₀₋₆
		alkyl- $\mathbb{R}^k$ ; and
25		(iii) optionally substituted with one or more substituents each of
		which is independently halogen, -OH, -CN, -O-C1-6 alkyl,
		-O-C ₁₋₆ haloalkyl, or -N(RaRb), or
	(21)	-C ₁₋₆ alkyl, substituted with -O-C ₁₋₆ alkyl, and with a substituent
30		selected from the group consisting of $-N(R^a)C(=0)R^k$ and $-N(R^a)C_{1-6}$ alkyl- $R^k$ ,
	R ² is -H or -C	C1-6 alkyl which is optionally substituted with one or more substituents
	each of which	is independently

(1) (2) halogen,
-OH,

	(0)	COT .
	(3)	-CN,
	(4)	-O-C ₁₋₆ alkyl,
	(5)	-O-C ₁₋₆ haloalkyl,
	(6)	$-C(=O)R^a$ ,
5	(7)	-CO ₂ Ra,
	(8)	-SR ^a ,
	(9)	-S(=O)R ^a ,
	(10)	-N(RaRb),
	(11)	-C(=O)N(RaRb),
10	(12)	$-N(R^a)-C(=O)-C_{1-6}$ alkyl $-N(R^bR^c)$ ,
	(13)	-SO ₂ R ^a ,
	(14)	-N(Ra)SO ₂ Rb,
	(15)	-SO ₂ N(RaRb),
	(16)	$-N(R^a)-C(R^b)=O$ ,
15	(17)	-C ₃₋₈ cycloalkyl,
	(18)	aryl, wherein the aryl is optionally substituted with one or more substituents each of which is independently halogen, -C1-6
		alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl,
		-C ₀₋₆ alkyl-N(R ^a R ^b ), or -C ₁₋₆ alkyl substituted with a 5-
20		or 6-membered saturated heterocyclic ring containing from
		1 to 4 heteroatoms independently selected from N, O and S
•		wherein the saturated heterocyclic ring is optionally
		substituted with from 1 to 3 substituents each of which is independently -C ₁₋₆ alkyl, oxo, or a 5- or 6-membered
25		heteroaromatic ring containing from 1 to 4 heteroatoms
		independently selected from N, O and S; or
	(19)	a 5- to 8-membered monocyclic heterocycle which is saturated
		or unsaturated and contains from 1 to 4 heteroatoms
		independently selected from N, O and S; wherein the
30		heterocycle is optionally substituted with one or more
		substituents each of which is independently -C1-6 alkyl,
•		-O-C ₁₋₆ alkyl, oxo, phenyl, or naphthyl;

R³ is -H or -C₁₋₆ alkyl;

### R4 is

(1) H,

(2) C₁₋₆ alkyl which is optionally substituted with one or more substituents each of which is independently halogen, -OH, O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -NO₂, -N(RaRb), -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -SO₂Ra, or -N(Ra)CO₂Rb,

(3) C₁₋₆ alkyl which is optionally substituted with one or more substituents each of which is independently halogen, -OH, or O-C₁₋₄ alkyl, and which is substituted with 1 or 2 substituents each of which is independently:

- (i) C₃₋₈ cycloalkyl,
- (ii) aryl,
- (iii) a fused bicyclic carbocycle consisting of a benzene ring fused to a C5.7 cycloalkyl,
- (iv) a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S,
- (v) a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or
- (vi) a 9- or 10-membered fused bicyclic heterocycle containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein at least one of the rings is aromatic,
- (4) C2-5 alkynyl optionally substituted with aryl,
- (5) C3_8 cycloalkyl optionally substituted with aryl,
- (6) aryl,
- (7) a fused bicyclic carbocycle consisting of a benzene ring fused to a C5-7 cycloalkyl,
- (8) a 5- or 6-membered saturated heterocyclic ring containing from
   1 to 4 heteroatoms independently selected from N, O and S,
- (9) a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or

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(10) a 9- or 10-membered fused bicyclic heterocycle containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein at least one of the rings is aromatic;

### wherein

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each aryl in (3)(ii) or the aryl (4), (5) or (6) or each fused carbocycle in (3)(iii) or the fused carbocycle in (7) is optionally substituted with one or more substituents each of which is independently halogen, -OH, -C1-6 alkyl, -C1-6 alkyl-ORa, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, -CN, -NO2, -N(RaRb), -C1-6 alkyl-N(RaRb), -C(=O)N(RaRb), -C(=O)Ra, -CO2Ra, -C1-6 alkyl-CO2Ra, -OCO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), -N(Ra)C(=O)Rb, -N(Ra)CO2Rb, -C1-6 alkyl-N(Ra)CO2Rb, aryl, -C1-6 alkyl-aryl, -O-aryl, or -C0-6 alkyl-het wherein het is a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, and het is optionally fused with a benzene ring, and is optionally substituted with one or more substituents each of which is independently -C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, oxo, or -CO2Ra;

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each saturated heterocyclic ring in (3)(iv) or the saturated heterocyclic ring in (8) is optionally substituted with one or more substituents each of which is independently halogen, -C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, oxo, aryl, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and

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each heteroaromatic ring in (3)(v) or the heteroaromatic ring in (9) or each fused bicyclic heterocycle in (3)(vi) or the fused bicyclic heterocycle in (10) is optionally substituted with one or more substituents each of which is independently halogen, -C1-6 alkyl, -C1-6 haloalkyl, -O-C1-6 alkyl, -O-C1-6 haloalkyl, oxo, aryl, or -C1-6 alkyl-aryl;

or alternatively R³ and R⁴ together with the N to which both are attached form a C₃₋₇ azacycloalkyl which is optionally substituted with one or more substituents each of which is independently -C₁₋₆ alkyl or oxo;

each Ra, Rb, Rc, and Rd is independently -H or -C1-6 alkyl;

Rk is carbocycle or heterocycle, wherein the carbocycle or heterocycle is optionally

5 substituted with one or more substituents each of which is independently (1) halogen, (2) -OH, -CN, (3) -C₁₋₆ alkyl, which is optionally substituted with one or more (4) 10 substituents each of which is independently halogen, -OH, -CN, -O-C1-6 alkyl, -O-C1-6 haloalkyl, -C(=O)Ra,  $-CO_2Ra$ , -SRa, -S(=O)Ra, -N(RaRb),  $-C(=O)-(CH_2)_{0-2}N(R^aR^b),$  $N(R^a)-C(=O)-(CH_2)_{0-2}N(R^bR^c)$ , -SO₂Ra  $-N(R^a)SO_2R^b$ ,  $-SO_2N(R^aR^b)$ , or  $-N(R^a)-C(R^b)=O$ , 15 (5) -O-C1-6 alkyl, which is optionally substituted with one or more substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -C(=O)Ra,  $-CO_2Ra$ , -SRa, -S(=O)Ra, -N(RaRb), 20  $-C(=O)-(CH_2)_{0-2}N(R^aR^b),$  $N(R^a)-C(=0)-(CH_2)_{0-2}N(R^bR^c), -SO_2R^a$  $-N(Ra)SO_2Rb$ ,  $-SO_2N(RaRb)$ , or -N(Ra)-C(Rb)=O. (6) -NO₂, **(7)** 25 ethylenedioxy, spiro substituted on a ring carbon in a saturated (8) ring of Rk; (9) -C(=O)Ra(10)-CO₂Ra, (11)-SRa, 30 (12)-S(=O)Ra(13)-N(RaRb), -C(=O)N(RaRb),(14)(15) $-C(=O)-C_{1-6}$  alkyl-N(RaRb),

(16)

(17)

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-N(Ra)C(=O)Rb

-SO₂Ra,

	(18)	-SO ₂ N(RaRb),
	(19)	-N(Ra)SO ₂ Rb,
	(20)	-R ^m ,
	(21)	-C ₁₋₆ alkyl-Rm, wherein the alkyl is optionally substituted with
5		one or more substituents each of which is independently halogen, -OH, -CN, -C1-6 haloalkyl, -O-C1-6 alkyl,
		-O-C ₁₋₆ haloalkyl, -C(=O)Ra, -CO ₂ Ra, -SRa,
		$-S(=O)Ra$ , $-N(RaRb)$ , $-N(Ra)CO_2Rb$ , $-SO_2Ra$ ,
		$-N(R^a)SO_2R^b$ , $-SO_2N(R^aR^b)$ , or $-N(R^a)-C(R^b)=O$ ,
10	(22)	-C ₀₋₆ alkyl-N(R ^a )-C ₀₋₆ alkyl-R ^m ,
	(23)	-C ₀₋₆ alkyl-O-C ₀₋₆ alkyl-R ^m ,
	(24)	-C ₀₋₆ alkyl-S-C ₀₋₆ alkyl-R ^m ,
	(25)	$-C_{0-6}$ alkyl- $C(=0)$ - $C_{0-6}$ alkyl- $R^m$ ,
	(26)	-C(=O)-O-C ₀₋₆ alkyl-R ^m ,
15	(27)	$-C(=O)N(R^a)-C_{0-6}$ alkyl- $R^m$ ,
	(28)	-N(Ra)C(=O)-Rm
	(29)	-N(Ra)C(=0)-C ₁₋₆ alkyl-Rm, wherein the alkyl is optionally
		substituted with one or more substituents each of which is independently halogen, -OH, -CN, -C1-6 haloalkyl,
20		-O-C ₁₋₆ alkyl, -O-C ₁₋₆ haloalkyl, -C(=O)R ^a , -CO ₂ R ^a , -SR ^a , -S(=O)R ^a , -N(R ^a R ^b ), -N(R ^a )CO ₂ R ^b , -SO ₂ R ^a , -N(R ^a )SO ₂ R ^b , -SO ₂ N(R ^a R ^b ), or -N(R ^a )-C(R ^b )=O,
	(20)	-N(Ra)-C(=0)-N(Rb)-C0-6 alkyl-Rm,
	(30)	-N(Ra)-C(=O)-O-C ₀₋₆ alkyl-Rm, or
0.5	(31)	-N(Ra)-C(=O)-N(Rb)-SO ₂ -C ₀₋₆ alkyl-R ^m ;
25	(32)	-14(Va)-c(=0)-14(Va)-205-c0-0 gryl-var,

carbocycle in Rk is (i) a C3 to C8 monocyclic, saturated or unsaturated ring, (ii) a C7 to C12 bicyclic ring system, or (iii) a C11 to C16 tricyclic ring system, wherein each ring in (ii) or (iii) is independent of or fused to the other ring or rings and each ring is saturated or unsaturated;

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heterocycle in Rk is (i) a 4- to 8-membered, saturated or unsaturated monocyclic ring, (ii) a 7- to 12-membered bicyclic ring system, or (iii) an 11 to 16-membered tricyclic ring system; wherein each ring in (ii) or (iii) is independent of or fused to or bridged

with or spiro to the other ring or rings and each ring is saturated or unsaturated; the monocyclic ring, bicyclic ring system, or tricyclic ring system contains from 1 to 6 heteroatoms selected from N, O and S and a balance of carbon atoms; and wherein any one or more of the nitrogen and sulfur heteroatoms is optionally be oxidized, and any one or more of the nitrogen heteroatoms is optionally quaternized;

each R^m is independently C₃₋₈ cycloalkyl; aryl; a 5- to 8-membered monocyclic heterocycle which is saturated or unsaturated and contains from 1 to 4 heteroatoms independently selected from N, O and S; or a 9- to 10-membered bicyclic heterocycle which is saturated or unsaturated and contains from 1 to 4 heteroatoms independently selected from N, O and S; wherein any one or more of the nitrogen and sulfur heteroatoms in the monocyclic or bicyclic heterocycle is optionally oxidized and any one or more of the nitrogen heteroatoms is optionally quaternized; and wherein

the cycloalkyl or the aryl is optionally substituted with one or more substituents each of which is independently halogen, -C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -N(R^aR^b), aryl, or -C₁₋₆ alkyl-aryl; and

the monocyclic or bicyclic heterocycle is optionally substituted with one or more substituents each of which is independently halogen, -C₁₋₆ alkyl optionally substituted with -O-C₁₋₆ alkyl, -C₁₋₆ haloalkyl, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, oxo, aryl, -C₁₋₆ alkyl-aryl, -C(=O)-aryl, -CO₂-aryl, -CO₂-C₁₋₆ alkyl-aryl, a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and

each n is independently an integer equal to zero, 1 or 2;

or a pharmaceutically acceptable salt thereof.

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- 2. The compound according to claim 1, wherein  $R^1$  is:
- (1) -H,
  (2) -C₁₋₆ alkyl, which is optionally substituted with from 1 to 5
  substituents each of which is independently halogen, -OH, -CN,

$$\begin{split} &-\text{O-C}_{1\text{-}4} \text{ alkyl, -O-C}_{1\text{-}4} \text{ haloalkyl, -C(=O)} \\ &\text{R}^a, -\text{CO}_2 \\ &\text{R}^a, -\text{N(R}^a \\ &\text{R}^b), -\text{C(=O)-(CH}_2)_{0\text{-}2} \\ &\text{N(R}^a) - \text{C(=O)-(CH}_2)_{0\text{-}2} \\ &\text{N(R}^a) - \text{C(=O)-(CH}_2)_{0\text{-}2} \\ &\text{N(R}^a) - \text{C(=O)-(CH}_2)_{0\text{-}2} \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) \\ &\text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) - \text{N(R}^a) -$$

 $-SO_2N(RaRb)$ , -N(Ra)-C(=O)Rb,

 $-N(R^a)C(=O)N(R^bR^c)$ ,  $-N(R^a)C(=O)C(=O)N(R^bR^c)$ , or  $-N(R^a)C(=O)OR^b$ ,

 $(3) -R^k,$ 

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- (4) -C₁₋₄ alkyl-R^k, wherein the alkyl is optionally substituted with 1 or 2 substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -N(RaRb), or -N(Ra)-(CH₂)₂₋₄-OH,
- (5)  $-O-(CH_2)_{0-3}-R^k$ ,
- (6)  $-C_{1-4}$  alkyl-O-(CH₂)₀₋₃-R^k,
- (7)  $-(CH_2)_{0-3}-S(O)_{n}-(CH_2)_{0-3}-R^{k}$ ,
- (8)  $-O-(CH_2)_{1-3}-OR^k$ ,
- 15 (9) -O-(CH₂)₁₋₃-O-(CH₂)₁₋₃-R^k,
  - (10)  $-O-(CH_2)_{1-3}-S(O)_nR^k$ ,
  - (11)  $-(CH_2)_{0-3}-N(R^a)-R^k$ ,
  - (12)  $-(CH_2)_{0-3}-N(R^a)-(CH_2)_{1-3}-R^k$ ,
  - (13)  $-(CH_2)_{0-3}-N(R^a)-(CH_2)_{1-3}-OR^k$ ,
- 20 (14)  $-(CH_2)_{0-3}-C(=O)-R^k$ ,
  - (15)  $-(CH_2)_{0-3}-C(=O)N(R^a)-(CH_2)_{0-3}-R^k$ ,
  - (16)  $-(CH_2)_{0-3}-N(R_a)C(=O)-(CH_2)_{0-3}-R^k$ ,
  - (17)  $-(CH_2)_{0-3}-N(R^a)C(=O)-O-(CH_2)_{0-3}-R^k$ ,
  - (18) -C₁₋₆ alkyl which is:

25 (i) substituted with aryl or -O-aryl, wherein the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -OH, -C1-4 alkyl, -C1-4 alkyl-ORa, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl,

methylenedioxy attached to two adjacent carbon atoms, or aryl;

(ii) substituted with -R^k, -(CH₂)₁₋₃-R^k, -N(R^a)-C(=O)-(CH₂)₀₋₃-R^k, -(CH₂)₀₋₃-N(R^a)-(CH₂)₀₋₃-R^k, WO 03/035076

or -(CH₂)₀₋₃-O-(CH₂)₀₋₃-R^k, or -(CH₂)₀₋₃-N(R^a)-C(=O)-(CH₂)₀₋₃-R^k; and

- (iii) optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, or -N(R^aR^b),
- (19)  $-C(CH_3)_2N(R_a)C(=O)OCH_2R_k$ ,
- (20)  $-C(CH_3)_2N(R^a)CH_2R^k$ ,
- (21)  $-C(CH_3)_2N(R^a)C(=O)R^k$ ,
- (22)  $-C(R^b)(N(R^a)C(=O)R^k)(CH_2OR^c)$ , or
- 10 (23)  $-C(R^b)(N(R^a)(CH_2)-R^k)(CH_2OR^c)$ ,

or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 2, wherein R¹ is:

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(1) -H,

(2) -C₁-4 alkyl, which is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -OH, -CN, -O-C₁-4 alkyl, -O-C₁-4 haloalkyl, -C(=O)R^a, -CO₂R^a, -SR^a, -S(=O)R^a, -N(R^aR^b), -C(=O)-(CH₂)₀-2N(R^aR^b), N(R^a)-C(=O)-(CH₂)₀-2N(R^bR^c), -SO₂R^a, -N(R^a)SO₂R^b,

 $-SO_2N(RaRb)$ , -N(Ra)-C(=O)Rb,

-N(Ra)C(=O)N(RbRc), -N(Ra)C(=O)C(=O)N(RbRc), or -N(Ra)C(=O)ORb,

25 (3)

- (3) -R^k, (4) -CH(CH₃)-R^k,
- (5) -(CH₂)₁₋₄-R^k, wherein the -(CH₂)₁₋₄- moiety is optionally substituted with one of -N(R^aR^b) or -N(R^a)-(CH₂)₂-OH,
- (6)  $-(CH_2)_{1-2}-O-(CH_2)_{0-1}-R^k$ ,

30 (7)  $-(CH_2)_{1-2}-S(O)_{n}-(CH_2)_{0-1}-R^{k}$ ,

- (8)  $-O-(CH_2)_{1-2}-OR^k$ ,
- (9)  $-O-(CH_2)_{1-2}-O-(CH_2)_{1-2}-R^k$ ,

	(10)	-O-(CI	$H_2)_{1-2}-S(O)_nR^k$ ,
	(11)	-(CH ₂	$_{1-2}$ -N(Ra)-Rk,
	(12)		) ₁₋₂ -N(R ^a )-(CH ₂ ) ₁₋₃ -R ^k ,
	(13)	-(CH2	) ₁₋₂ -N(R ^a )-(CH ₂ ) ₁₋₃ -OR ^k ,
5	(14)		) ₀₋₂ -C(=0)-R ^k ,
	(15)		)N(R ^a )-(CH ₂ ) ₁ -2-R ^k ,
	(16)		$_{0-2}$ -C(=O)N(R ^a )-(CH ₂ ) ₀₋₂ -R ^k ,
	(17)		) ₁₋₂ -N(R ^a )C(=O)-(CH ₂ ) ₀₋₁ -R ^k ,
	(18)	-(CH ₂	$_{1-2}$ -N( $\tilde{R}^{a}$ )C(=O)-O-(CH ₂ ) ₀₋₁ - $R^{k}$ ,
10	(19)	-C1-4	alkyl which is:
		(i)	substituted with aryl or -O-aryl wherein the aryl is optionally
			substituted with from 1 to 3 substituents each of which is
			independently fluoro, chloro, -C1-4 alkyl, -C1-4 fluoroalkyl,
			-O-C ₁₋₄ alkyl, -O-C ₁₋₄ fluoroalkyl, methylenedioxy attached
15			to two adjacent carbon atoms, or phenyl;
		(ii)	substituted with -Rk, -(CH2)1-3-Rk,
			-N(Ra)-C(=O)-(CH ₂ ) ₀₋₃ -R ^k , -N(Ra)-(CH ₂ ) ₁₋₃ -R ^k ,
			-O-(CH ₂ ) ₁₋₂ -R ^k , or -N(R ^a )-C(=O)-(CH ₂ ) ₀₋₂ -R ^k ; and
		(iii)	optionally substituted with from 1 to 4 substituents each of
20			which is independently halogen, -OH, -CN, -O-C1-4 alkyl,
			-O-C ₁₋₄ haloalkyl, or -N(RaRb),
	(20)		$H_3)_2N(R^a)C(=O)OCH_2R^k$
	(21)		H ₃ ) ₂ N(R ^a )CH ₂ R ^k ,
	(22)		$H_3)_2N(R^a)C(=O)R^k$
25	(23)		o)(N(Ra)C(=O)Rk)(CH2ORc), or
	(24)	•	o)(N(Ra)(CH ₂ )-R ^k )(CH ₂ ORc),
or a pharmaceutically acceptable salt thereof.			

4. The compound according to claim 1, wherein

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Rk is C3-8 cycloalkyl; aryl selected from phenyl and naphthyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms

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independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S;

wherein the cycloalkyl, aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 4 substituents each of which is independently

- (1) halogen,
- (2) -OH,
- (3) -CN,
- 10 (4) -C₁₋₄ haloalkyl,
  - (5) -C₁₋₄ alkyl, which is optionally substituted with from 1 to 3 substituents each of which is independently -OH, -CN, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)R^a, -CO₂R^a, -SR^a, -S(=O)R^a, -N(R^aR^b), -C(=O)-(CH₂)₀₋₂N(R^aR^b), N(R^a)-C(=O)-(CH₂)₀₋₂N(R^bR^c), -SO₂R^a, -N(R^a)SO₂R^b, -SO₂N(R^aR^b), or -N(R^a)-C(R^b)=O,
  - (6) -O-C₁₋₄ haloalkyl
  - (7) -O-C₁₋₄ alkyl, which is optionally substituted with from 1 to 3 substituents each of which is independently -OH, -CN, -O-C₁₋₆ alkyl, -O-C₁₋₆ haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-(CH₂)₀₋₂N(RaRb), N(Ra)-C(=O)-(CH₂)₀₋₂N(RbRc), -SO₂Ra, -N(Ra)SO₂Rb, -SO₂N(RaRb), or -N(Ra)-C(Rb)=O,
    - (8)  $-NO_2$ ,
- 25 (9) oxo,
  - (10)  $-C(=O)R^a$ ,
  - (11)  $-CO_2R^a$ ,
  - (12) -SRa,
  - (13)  $-S(=O)R^a$ ,
- 30  $(14) -N(R^{a}R^{b}),$ 
  - (15) -C(=O)N(RaRb),
  - (16)  $-C(=O)-C_{1-6}$  alkyl-N(RaRb),
  - (17)  $-N(R^a)C(=0)R^b$ ,
  - (18) -SO₂Ra,
- 35  $(18) -SO_2N(R^{a}R^{b}),$

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-N(Ra)SO2Rb,
                      (19)
                              -Rm,
                      (20)
                              -CH(CH3)-Rm,
                      (21)
                              -(CH_2)_{1-4}-Rm
                      (22)
                      (23)
                              -(CH<sub>2</sub>)<sub>0-2</sub>-N(Ra)-(CH<sub>2</sub>)<sub>0-2</sub>-Rm,
 5
                              -(CH2)0-2-O-(CH2)0-2-Rm,
                      (24)
                              -(CH<sub>2</sub>)<sub>0-2</sub>-S-(CH<sub>2</sub>)<sub>0-2</sub>-Rm,
                      (25)
                              -(CH_2)_{0-2}-C(=O)-(CH_2)_{0-2}-R^m
                      (26)
                              -C(=O)-O-(CH2)0-2-Rm,
                      (27)
                              -C(=O)N(R^a)-R^m
                      (28)
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                               -N(Ra)C(=O)-Rm,
                      (29)
                               -N(Ra)C(=O)-(CH2)1-3-Rm, wherein the -(CH2)1-3- moiety is
                      (30)
                                      optionally substituted with one of -N(RaRb),
                                      -N(Ra)CO_2Rb, -SO_2Ra, -N(Ra)SO_2Rb, -SO_2N(RaRb),
                                      or -N(R^a)-C(R^b)=O,
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                              -N(Ra)-C(=O)-N(Rb)-(CH_2)_{1-2}-Rm,
                       (31)
                               -N(R^a)-C(=O)-O-(CH_2)_{1-2}-R^m, or
                      (32)
                               -N(R^a)-C(=O)-N(R^b)SO_2-R^m;
                       (33)
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- or a pharmaceutically acceptable salt thereof.
  - 5. The compound according to claim 4, wherein

each Rm is independently C5-7 cycloalkyl; aryl selected from phenyl and naphthyl; a

5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms
independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring
containing from 1 to 4 heteroatoms independently selected from N, O and S; or a
bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered, saturated or
unsaturated heterocyclic ring containing from 1 to 3 heteroatoms selected from N, O

30 and S; wherein

the cycloalkyl or the aryl is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -N( $R^aR^b$ ), phenyl, or -(CH2)1-2-phenyl;

the saturated heterocyclic ring is optionally substituted with from 1 to 4 substituents each of which is independently -C1-4 alkyl optionally substituted with -O-C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, oxo, phenyl, -(CH2)1-2-phenyl, -C(=O)-phenyl, -CO2-phenyl, -CO2-(CH2)1-2-phenyl, a 5- or 6-membered saturated heterocyclic ring

containing from 1 to 4 heteroatoms independently selected from N, O and S, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and

the heteroaromatic ring or the bicyclic heterocycle is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, oxo, phenyl, or -(CH₂)₁₋₂-phenyl;

or a pharmaceutically acceptable salt thereof.

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# 6. The compound according to claim 4, wherein

Rk is cycloalkyl selected from cyclopropyl, cyclopentyl and cyclohexyl; aryl selected from phenyl and naphthyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring selected from pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, pyranyl, tetrahydrofuranyl, imidazolidinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, and pyrazolidinyl; a 5- or 6-membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxopiperidinyl, oxazolyl, isooxazolyl, oxadiazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl; or a bicyclic heterocycle selected from indolyl, indolinyl, tetrahydroquinolinyl, quinolinyl, 1,4-dioxa-8-azaspiro[4.5]decyl, azabicyclo[2.2.1]heptyl, azabicyclo[2.1.1]hexyl, tetrahydroisoquinolinyl, isoquinolinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo-1,4-dioxinyl, and benzo-1,3-dioxolyl;

wherein the cycloalkyl, aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

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(1) fluoro,

		·
	(2)	chloro,
	(3)	bromo,
	(4)	
	(5)	-C ₁₋₄ alkyl, which is optionally substituted with 1 or 2
5		substituents each of which is independently -OH, -CN, -O-C ₁₋₄ alkyl, -OCF ₃ , -N(R ^a R ^b ), -C(=O)N(R ^a R ^b ), or N(R ^a )-C(=O)-(CH ₂ ) ₀₋₂ N(R ^b R ^c ),
	(6)	-OCF3,
	(7)	-O-C ₁₋₄ alkyl
10	(8)	-NO ₂ ,
	(9)	oxo,
	(10)	-C(=O)Ra,
	(11)	-CO ₂ Ra,
	(12)	-SR ^a ,
15	(13)	$-S(=O)R^a$ ,
	(14)	-N(RaRb),
		-C(=O)N(RaRb),
	(16)	$-C(=O)-(CH_2)_{1-2}-N(R^aR^b),$
	(17)	$-N(R^a)C(=O)R^b$ ,
20	(18)	-SO ₂ R ^a ,
	(19)	-R ^m ,
	(20)	-CH(CH3)-R ^m ,
	(21)	-CH ₂ -R ^m ,
	(22)	-(CH ₂ ) ₀₋₂ -N(R ^a )-(CH ₂ ) ₀₋₂ -R ^m ,
25	(23)	-O-(CH ₂ ) ₁ - ₂ -R ^m ,
	(24)	•
	(25)	-(CH2)0-1-C(=O)-(CH2)0-2-Rm,
	(26)	-(CH2)0-1-C(=O)-O-(CH2)0-2-Rm,
	(27)	$-C(=O)N(R^a)-R^m$
30	(28)	-N(Ra)C(=O)-Rm,
	(29)	-N(Ra)C(=0)-(CH2)1-2-Rm, wherein the -(CH2)1-2- moiety is
		optionally substituted with -N(RaRb),
	(30)	-N(Ra)-C(=O)-N(Rb)-(CH ₂ ) ₁₋₂ -Rm,
	(31)	-N(Ra)-C(=O)-O-(CH ₂ ) ₁ -2-R ^m ,
35	(32)	$-N(R^a)-C(=O)-N(R^b)SO_2-R^m$ ,

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## (33) -OH;

or a pharmaceutically acceptable salt thereof.

## 7. The compound according to claim 6, wherein

each Rm is independently aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperidinyl, piperazinyl, thiazolidinyl, and morpholinyl; or a 5- or 6-membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiadiazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(RaRb);

the saturated heterocyclic ring is optionally substituted with 1 or 2 substituents each of which is independently -C1_4 alkyl, -CF3, -O-C1_4 alkyl, -OCF3, oxo, phenyl, -(CH2)1-2-phenyl, -C(=O)-phenyl, -CO2-phenyl, or -CO2-CH2-phenyl; and

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, oxo, phenyl, or -(CH₂)₁₋₂-phenyl;

or a pharmaceutically acceptable salt thereof.

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- 8. The compound according to claim 1, wherein R² is -H or -C₁₋₆ alkyl which is optionally substituted with one of:
  - (1) -N(RaRb),
  - phenyl which is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, or -C₀₋₆ alkyl-N(RaRb), or
  - (3) a 5- or 6-membered saturated monocyclic heterocycle which contains from 1 to 4 heteroatoms independently selected from N, O and S; wherein the heterocycle is optionally substituted

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with from 1 to 4 substituents each of which is independently -C₁₋₆ alkyl, -O-C₁₋₆ alkyl, oxo, or phenyl;

or a pharmaceutically acceptable salt thereof.

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- 9. The compound according to claim 8, wherein R² is
- (1) -H,
- (2) -C₁₋₄ alkyl,
- (3)  $-(CH_2)_{1-3}-N(R^aR^b)$ ,

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- (4) -(CH₂)₁₋₃-phenyl, wherein the phenyl is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, chloro, bromo, -C₁₋₄ alkyl, -C₁₋₄ fluoroalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ fluoroalkyl, or -(CH₂)₁₋₃-N( $R^aR^b$ ); or
- (5) -(CH₂)₁₋₃R^t, wherein R^t is a 6-membered saturated

  15 heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N,

  O and S;

or a pharmaceutically acceptable salt thereof.

- 20 10. The compound according to claim 9, wherein R² is -H or methyl; or a pharmaceutically acceptable salt thereof.
  - 11. The compound according to claim 10, wherein R² is -H; or a pharmaceutically acceptable salt thereof.

- 12. The compound according to claim 1, wherein R³ is -H or -C₁₋₄ alkyl; or a pharmaceutically acceptable salt thereof.
- 13. The compound according to claim 12, wherein R³ is -H or methyl; or a pharmaceutically acceptable salt thereof.
  - 14. The compound according to claim 13, wherein R³ is -H; or a pharmaceutically acceptable salt thereof.
- 35 15. The compound according to claim 1, wherein R⁴ is

	•	(1)	C ₁ _4 aikyi,
	•	(2)	C ₁₋₄ alkyl substituted with from 1 to 3 substituents each of
			which is independently -OH, O-C ₁₋₄ alkyl, or -O-C ₁₋₄
5			haloalkyl,
•	1. · · · · ·	(3)	C ₁₋₄ alkyl which is substituted with an aryl or with two aryls
			which are the same or different, and is optionally substituted
÷ ;	•		with -OH,
		(4)	C ₁₋₄ alkyl substituted with one of:
10			(i) C5-7 cycloalkyl,
			(ii) a fused bicyclic carbocycle consisting of a benzene ring fused to a C5-7 cycloalkyl,
٠			(iii) a 5- or 6-membered saturated heterocyclic ring
			containing from 1 to 4 heteroatoms
15	•		independently selected from N, O and S,
15			(iv) a 5- or 6-membered heteroaromatic ring
			containing from 1 to 4 heteroatoms
		1.	independently selected from N, O and S, or
*			
			(v) a 9- or 10-membered fused bicyclic heterocycle containing from 1 to 4 heteroatoms
20		•	independently selected from N, O and S,
			wherein at least one of the rings is aromatic;
		(5)	C ₂₋₄ alkynyl optionally substituted with aryl,
	**. *	(5)	C ₂₋₇ cycloalkyl optionally substituted with aryl,
		(6)	•
25		(7)	aryl,
•	*	(8)	a fused bicyclic carbocycle consisting of a benzene ring fused
			to a C5-7 cycloalkyl,
		(9)	a 5- or 6-membered saturated heterocyclic ring containing from
			1 to 4 heteroatoms independently selected from N, O and S,
30	. •	(10)	a 5- or 6-membered heteroaromatic ring containing from 1 to 4
			heteroatoms independently selected from N, O and S, or
•		(11)	a 9- or 10-membered fused bicyclic heterocycle containing
			from 1 to 4 heteroatoms independently selected from N, O and
	•		S, wherein at least one of the rings is aromatic;
35		where	in

each aryl in (3) or the aryl in (5), (6) or (7) or the fused carbocycle in (4)(ii) or (8) is optionally substituted with from 1 to 4 substituents each of which is independently halogen. -OH. - $C_{1-4}$  alkyl, - $C_{1-4}$  alkyl- $OR^a$ , - $C_{1-4}$  haloalkyl, - $O-C_{1-4}$  alkyl, -O-C₁₋₄ haloalkyl, -CN, -NO₂, -N(RaRb), -C₁₋₄ 5 alkyl-N(RaRb), -C(=O)N(RaRb), -C(=O)Ra, -CO2Ra, -C1-4 alkyl-CO2Ra, -OCO2Ra, -SRa, -S(=O)Ra, -SO2Ra,  $-N(Ra)SO_2Rb$ ,  $-SO_2N(RaRb)$ , -N(Ra)C(=O)Rb, -N(Ra)CO2Rb, -C1-4 alkyl-N(Ra)CO2Rb, phenyl, -C1-4 alkyl-phenyl, -O-phenyl, or -(CH2)0-2-het wherein het is a 5-10 or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, and het is optionally fused with a benzene ring, and is optionally substituted with 1 or 2 substituents each of which is independently -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, 15 -O-C₁₋₄ haloalkyl, or -CO₂Ra; the saturated heterocyclic ring in (4)(iii) or (9) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, oxo, phenyl, or a 5- or 6-20 membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and the heteroaromatic ring in (4)(iv) or (10) or the fused bicyclic heterocycle in (4)(v) or (11) is optionally substituted with from 1 to 4 substituents each of which is independently 25 halogen, -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4

or a pharmaceutically acceptable salt thereof.

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16. The compound according to claim 15, wherein R⁴ is:

haloalkyl, oxo, or phenyl;

- (1) C₁₋₃ alkyl substituted with 1 or 2 phenyls, and is optionally substituted with an -OH,
- 35 (2) C₁₋₄ alkyl substituted with one of:

- (i) cyclohexyl,
- (ii) naphthyl,
- (iii) a fused bicyclic carbocycle selected from

$$\begin{array}{c} z^1 \\ z^1 \\ z^1 \\ \end{array}$$

- (iv) a saturated heterocyclic ring containing from zero to 1 oxygen atoms and from 1 to 3 nitrogen atoms,
- (v) a 5- or 6-membered heteroaromatic ring containing from zero to 1 heteroatoms selected from O and S and from 1 to 3 nitrogen atoms, or
- (vi) a fused bicyclic heterocycle selected from

- (3)  $--(CH_2)_{1-2}$   $C = C R^u$  wherein  $R^u$  is H or phenyl,
  - (4) C₃₋₆ cycloalkyl optionally substituted with phenyl,
  - (5) phenyl or naphthyl,
  - (6) a fused bicyclic carbocycle selected from

$$\begin{array}{c} Z^1 \\ Z^2 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\ Z^1 \\$$

(7) a saturated heterocyclic ring containing from zero to 1 oxygen atoms and from 1 to 3 nitrogen atoms,

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(8) a 5- or 6-membered heteroaromatic ring containing from zero to 1 heteroatoms selected from O and S and from 1 to 3 nitrogen atoms, or

(9) a fused bicyclic heterocycle selected from

wherein Z1 is -H or -OH;

each phenyl in (1) or the phenyl in (3) or (4) or (5) or the naphthyl in (2)(ii) or (5) is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, bromo, chloro, -OH, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, -CN, -NO2, -(CH2)1-2-N(RaRb), -C(=O)Ra, -CO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), or -N(Ra)CO2Rb; and is additionally and optionally mono-substituted with phenyl, -(CH2)1-2-phenyl, -O-phenyl, or -(CH2)0-2-het wherein het is thiadiazolyl or indolyl, and het is optionally substituted with -C1-4 alkyl, -CF3, -O-C1-6 alkyl, -OCF3, or -CO2Ra;

the saturated heterocyclic ring in (2)(iv) or (7) is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, oxo; and is additionally and optionally mono-substituted with phenyl or a heteroaromatic ring selected from pyridyl, pyrimidinyl, and pyrazinyl; and

the heteroaromatic ring in (2)(v) or (8) is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, or oxo; and is additionally and optionally mono-substituted with phenyl;

or a pharmaceutically acceptable salt thereof.

17. The compound according to claim 15, wherein R4 is:

#### wherein

Q is ethynyl optionally substituted with aryl, (1) 5 (2) C₅₋₇ cycloalkyl, (3) aryl, a fused bicyclic carbocycle consisting of a benzene ring fused to a (4) C₅₋₇ cycloalkyl, a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 (5) 10 heteroatoms independently selected from N, O and S, a 5- or 6-membered heteroaromatic ring containing from 1 to 4 (6) heteroatoms independently selected from N, O and S, or a 9- or 10-membered fused bicyclic heterocycle containing from 1 to 4 (7) heteroatoms independently selected from N, O and S, wherein at least 15 one of the rings is aromatic;

wherein

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aryl in (1) or (3) or the fused carbocycle in (4) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -C1-4 alkyl, -C1-4 alkyl-ORa, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -CN, -NO2, -N(RaRb), -C1-4 alkyl-N(RaRb), -C(=O)N(RaRb), -C(=O)Ra, -CO2Ra, -C1-4 alkyl-CO2Ra, -OCO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), -N(Ra)C(=O)Rb, -N(Ra)CO2Rb, -C1-4 alkyl-N(Ra)CO2Rb, phenyl, -C1-4 alkyl-phenyl, -O-phenyl, or -(CH2)0-2-het wherein het is a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, and het is optionally fused with a benzene ring, and is optionally substituted with -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, or -CO2Ra;

the saturated heterocyclic ring in (5) is optionally substituted with from 1 to 4 substituents each of which is independently halogen,

-C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, oxo, phenyl, or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; and

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the heteroaromatic ring in (6) or the fused bicyclic heterocycle in (7) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C1-4 alkyl, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, oxo, or phenyl;

R⁵ is H, methyl, or CH₂OH, with the proviso that when R⁵ is CH₂OH, then Q is aryl; and

p is an integer equal to zero, 1 or 2;

or a pharmaceutically acceptable salt thereof.

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18. The compound according to claim 17, wherein Q is

- (1) —C≡C-R^u wherein R^u is H or phenyl,
- (2) phenyl or naphthyl,

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- (3) cyclopentyl or cyclohexyl,
- (4) a fused bicyclic carbocycle selected from the group consisting of indanyl, tetrahydronaphthalenyl, and benzocycloheptyl,
- (5) a saturated heterocyclic ring selected from the group consisting of tetrahydrofuranyl, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, and pyrazolidinyl,
- (6) a heteroaromatic ring selected from the group consisting of thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, oxadiazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl, or

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(7) a fused bicyclic heterocycle selected from the group consisting of benzothiophenyl, indolyl, pyridoimidazolyl, indazolyl, 2,3-dihydrobenzo-1,4-dioxinyl, dihydrobenzofuranyl, benzo-1,3-dioxolyl, quinolinyl, and isoquinolinyl;

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#### wherein

the phenyl in (1) or the phenyl or naphthyl in (2) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -C1_4 alkyl, -C1_4 haloalkyl, -O-C1_4 alkyl, -O-C1_4 haloalkyl, -CN, -NO2, -C1_4 alkyl-N(RaRb), -C(=O)Ra, -CO2Ra, -C1_4 alkyl-CO2Ra, -SRa, -S(=O)Ra, -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), -N(Ra)CO2Rb, -C1_4 alkyl-N(Ra)CO2Rb, phenyl, -(CH2)1_2-phenyl, -O-phenyl, or -(CH2)0_2-het wherein het is pyrrolyl, pyrazolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isothiazolyl, isooxazolyl, pyridyl, pyrazinyl, thiadiazolyl or indolyl, and het is optionally substituted with -C1_4 alkyl, -CF3, -O-C1_6 alkyl, -OCF3, oxo, or -CO2Ra;

the fused carbocycle in (4) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -OH, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C₁₋₄ alkyl-N(R^aR^b), -C(=O)R^a, -CO₂R^a, -SR^a, -S(=O)R^a, -SO₂R^a, -N(R^a)CO₂R^b, phenyl, -(CH₂)₁₋₂-phenyl, or -O-phenyl;

the saturated heterocyclic ring in (5) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, oxo, phenyl, pyridyl, pyrazinyl, or pyrimidinyl; and

the heteroaromatic ring in (6) or the fused bicyclic heterocycle in (7) is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C1_4 alkyl, -C1_4 haloalkyl, -O-C1_4 alkyl, -O-C1_4 haloalkyl, oxo, or phenyl;

or a pharmaceutically acceptable salt thereof.

The compound according to claim 18, wherein Q is phenyl, which is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, bromo, chloro, -OH, -C₁₋₄ alkyl, -C₁₋₄ fluoroalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ fluoroalkyl, -CN, -SRa, -(CH₂)₁₋₂-N(RaRb), -SO₂Ra, -N(Ra)SO₂Rb, -SO₂N(RaRb), -(CH₂)₀₋₂-CO₂Ra*, -(CH₂)₀₋₂-N(Ra)CO₂Rb*, -NO₂, or phenyl;

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35 each Ra is independently H, methyl, or ethyl;

each Rb is independently H, methyl, or ethyl; and

each Ra* and Rb* is independently H or -C1-4 alkyl;

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or a pharmaceutically acceptable salt thereof.

 $20. \qquad \text{The compound according to claim 19, wherein $R^5$ is $H$ and $p$ is} \\ \text{zero; or a pharmaceutically acceptable salt thereof.}$ 

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21. The compound according to claim 20, wherein Q is phenyl which is optionally substituted with from 1 to 3 substituents, each of which is independently -F, -Br, -Cl, -OH, -C1-4 alkyl, -C1-4 fluoroalkyl, -O-C1-4 alkyl, -O-C1-4 fluoroalkyl, -CN, -SRa or -SO2Ra;

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or a pharmaceutically acceptable salt thereof.

22. The compound according to claim 21, wherein Q is p-fluorophenyl or 2,3-dimethoxyphenyl;

20

or a pharmaceutically acceptable salt thereof.

23. The compound according to claim 1, wherein

25  $R^1$  is  $-R^k$ ;

Rk is a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms independently selected from N, O and S;

wherein the heteroaromatic ring is optionally substituted with from 1 to 30 3 substituents each of which is independently

- (1) halogen,
- -C₁₋₆ alkyl, which is optionally substituted with from 1 to 5 substituents each of which is independently halogen,
  -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)Ra, -CO₂Ra,
  -SRa, -S(=O)Ra, -N(RaRb), -C(=O)-(CH₂)0-2N(RaRb),

N(Ra)-C(=O)-(CH2)0-2N(RbRc), -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), or -N(Ra)-C(Rb)=O,

		(3)	-NO ₂ ,
		(4)	oxo,
5		(5)	-C(=O)Ra,
		(6)	-CO ₂ Ra,
		(7)	-C(=O)N(RaRb),
		(8)	$-C(=O)-C_1$ -4 alkyl-N(RaRb),
		(9)	-R ^m ,
10		(10)	-C ₁₋₆ alkyl-Rm, wherein the alkyl is optionally substituted with
	1.		from 1 to 5 substituents each of which is independently
			halogen, -OH, -CN, -C1_4 haloalkyl, -O-C1_4 alkyl,
		• .	-O-C ₁₋₄ haloalkyl, -C(=O)Ra, -CO ₂ Ra, -SRa,
			$-S(=O)Ra$ , $-N(RaRb)$ , $-N(Ra)CO_2Rb$ , $-SO_2Ra$ ,
15		•	$-N(R^a)SO_2R^b$ , $-SO_2N(R^aR^b)$ , or $-N(R^a)-C(R^b)=O$ ,
		(11)	-C ₀₋₄ alkyl-N( $R^a$ )-C ₀₋₄ alkyl- $R^m$ ,
·	•	(12)	- $C_{0-4}$ alkyl- $O$ - $C_{0-4}$ alkyl- $R^m$ ,
		(13)	-C ₀₋₄ alkyl-S-C ₀₋₄ alkyl-R ^m ,
•		(14)	$-C_{0-4}$ alkyl-C(=0)-C ₀₋₄ alkyl-R ^m ,
20		(15)	-C(=O)-O-C ₀₋₄ alkyl-R ^m ,
		(16)	$-C(=O)N(R^a)-C_{0-4}$ alkyl- $R^m$ ,
		(17)	$-N(R^a)C(=O)-R^m$
		(18)	-N(Ra)C(=O)-C1-6 alkyl-Rm, wherein the alkyl is optionally
	,		substituted with from 1 to 5 substituents each of which
25			is independently halogen, -OH, -CN, -C1-4 haloalkyl,
	<b>.</b>		-O-C ₁₋₄ alkyl, -O-C ₁₋₄ haloalkyl, -C(=O)Ra, -CO ₂ Ra,
			$-SRa$ , $-S(=O)Ra$ , $-N(RaRb)$ , $-N(Ra)CO_2Rb$ , $-SO_2Ra$ ,
•	•		$-N(Ra)SO_2R^b$ , $-SO_2N(RaR^b)$ , or $-N(Ra)-C(R^b)=O$ ,
		(19)	$-N(R^a)-C(=O)-N(R^b)-C_{0-4}$ alkyl- $R^m$ ,
30		(20)	-N( $R^a$ )-C(=O)-O-C ₀₋₄ alkyl- $R^m$ , or
		(21)	$-N(R^a)-C(=O)-N(R^b)SO_2-C_{0-4}$ alkyl- $R^m$ ;

wherein each Rm is independently aryl selected from phenyl and naphthyl or a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(RaRb); and

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently - $C_{1-4}$  alkyl or oxo; and

10 each Ra and Rb is independently -H or -C1-4 alkyl;

or a pharmaceutically acceptable salt thereof.

24. The compound according to claim 23, wherein R¹ is:

Rба is:

(1) 
$$-H$$
,

O  $X^2$ 
 $Y^1$ 

O  $Y^1$ 

O  $Y^1$ 

O  $Y^1$ 

O  $Y^1$ 

O  $Y^1$ 

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O

wherein  $X^1$  is a single bond connecting the carbonyl carbon to the carbon substituted with  $X^2$ , -O-, or -NH-;

 $X^2$  is -H, -NH₂, or -N(H)CO₂R^a;

Y¹ is -H, halo or -C₁₋₄ alkyl; and

r is an integer equal to zero, 1 or 2; and

R6b is -H or -NO2; and

R⁷ is -H or -C₁₋₄ alkyl;

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or a pharmaceutically acceptable salt thereof.

- 25. The compound according to claim 24, wherein
- 15 R6a and R6b are both -H; and

R⁷ is -H or -CH₃;

or a pharmaceutically acceptable salt thereof.

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26. The compound according to claim 25, wherein

R² is -H or methyl;

 $R^3$  is -H; and

R4 is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, -CN, or -SO₂R^a; and is additionally and optionally monosubstituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl,

30 substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

or a pharmaceutically acceptable salt thereof.

# 27. The compound according to claim 1, wherein:

R1 is -Rk;

Rk is phenyl which is optionally substituted with from 1 to 3 substituents each of 5 which is independently: halogen, (1)-C1-6 alkyl, which is optionally substituted with from 1 to 5(2)substituents each of which is independently halogen, -OH, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)Ra, 10  $-CO_2Ra$ , -SRa, -S(=O)Ra, -N(RaRb),  $-C(=O)-(CH_2)_{0-2}N(R^aR^b),$  $N(R^a)-C(=O)-(CH_2)_{O-2}N(R^bR^c)$ , -SO₂R_a,  $-N(Ra)SO_2Rb$ ,  $-SO_2N(RaRb)$ , or -N(Ra)-C(Rb)=O, (3) -NO₂, 15  $-C(=O)R^a$ , (4) (5) -CO₂Ra, -C(=O)N(RaRb),(6)  $-C(=0)-C_{1-4}$  alkyl-N(RaRb), (7) -Rm, (8) 20 -C1-6 alkyl-Rm, wherein the alkyl is optionally substituted with (9) from 1 to 5 substituents each of which is independently halogen, -OH, -CN, -C1_4 haloalkyl, -O-C1_4 alkyl, -O-C₁₋₄ haloalkyl, -C(=O)Ra, -CO₂Ra, -SRa, -S(=O)Ra, -N(RaRb),  $-N(Ra)CO_2Rb$ ,  $-SO_2Ra$ , 25  $-N(Ra)SO_2Rb$ ,  $-SO_2N(RaRb)$ , or -N(Ra)-C(Rb)=O, -C₀₋₄ alkyl-N(Ra)-C₀₋₄ alkyl-Rm, (10)-C₀₋₄ alkyl-O-C₀₋₄ alkyl-R^m, (11)-C0_4 alkyl-S-C0_4 alkyl-Rm, (12) $-C_{0-4}$  alkyl-C(=O)-C₀₋₄ alkyl-R^m, 30 (13) $-C(=O)-O-C_{0-4}$  alkyl-Rm, (14) $-C(=O)N(R^a)-C_{0-4}$  alkyl-Rm, (15)-N(Ra)C(=O)-Rm, (16)

(17)

-N(Ra)C(=0)-C1-6 alkyl-Rm, wherein the alkyl is optionally

substituted with from 1 to 5 substituents each of which is independently halogen, -OH, -CN, -C1-4 haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, -C(=O)Ra, -CO2Ra, -SRa, -S(=O)Ra, -N(RaRb), -N(Ra)CO2Rb, -SO2Ra, -N(Ra)SO2Rb, -SO2N(RaRb), or -N(Ra)-C(Rb)=O,

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- (18)  $-N(R^a)-C(=O)-N(R^b)-C_{0-4}$  alkyl-Rm,
- (19) -N(Ra)-C(=O)-O-C₀₋₄ alkyl-Rm, or
- (20)  $-N(R^a)-C(=O)-N(R^b)SO_2-C_{0-4}$  alkyl- $R^m$ ;
- wherein each Rm is independently aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; or a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; wherein
  - the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(R^aR^b);

the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C₁-4 alkyl or oxo, and is additionally optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-(CH₂)₁₋₂-phenyl; and

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl or oxo;

or a pharmaceutically acceptable salt thereof.

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- 28. The compound according to claim 27, wherein  $\mathbb{R}^1$  is phenyl which is mono-substituted with one of:
  - (1) fluoro, chloro, or bromo,
  - -C₁₋₄ alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C₁₋₄ alkyl, -OCF₃, -C(=O)R^a, -CO₂R^a, -SR^a, -N(R^aR^b), or -C(=O)N(R^aR^b),
  - (3) -NO₂,
  - (4) -C₁₋₄ alkyl-Rm,
- 35 (5)  $-O-(CH_2)_{1-2}-R^m$ ,

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- (6)  $-(CH_2)_{0-2}-S-(CH_2)_{0-2}-R^m$ ,
- (7) -N(Ra)C(=O)-Rm,
- (8) -N(Ra)C(=O)-(CH2)1-2-Rm, wherein the (CH2)1-2 moiety is optionally mono-substituted with -N(RaRb) or -N(Ra)CO₂Rb, or
- (9)  $-N(R^a)-C(=O)-N(R^b)-(CH_2)_{1-2}-R^m;$

wherein Rm is aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing 1 or 2 heteroatoms independently selected from N and O; or a 5- or 6-membered heteroaromatic ring containing from 1 or 2 nitrogens; wherein the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C1-4 alkyl, -CF3, -O-C1-4 alkyl, -OCF3, or -N(RaRb); and

the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C₁₋₄ alkyl or oxo; and is additionally and optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-(CH₂)₁₋₂-phenyl; and

the heteroaromatic ring is optionally substituted with 1 or 2 substituents each of which is independently -C1_4 alkyl or oxo; and

each Ra and Rb is each independently -H or -C1-4 alkyl;

or a pharmaceutically acceptable salt thereof.

29. The compound according to claim 28, wherein

R² is -H or methyl;

R³ is -H; and

 $R^4$  is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, -CN, or -SO₂Ra; and is additionally and optionally mono-

substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

or a pharmaceutically acceptable salt thereof.

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30. The compound according to claim 1, wherein

R1 is -Rk;

10 Rk is a 5- or 6-membered saturated heterocyclic ring containing from 0 to 1 oxygen atoms and from 1 to 3 nitrogen atoms or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated heterocyclic ring containing from 0 to 1 oxygen atoms and from 1 to 3 nitrogen atoms;

wherein the saturated heterocyclic ring or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

- (1) halogen,
- -C₁₋₆ alkyl, which is optionally substituted with from 1 to 5 substituents each of which is independently halogen,
  -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)R^a, -CO₂R^a,
  -SR^a, -S(=O)R^a, -N(R^aR^b), -C(=O)-(CH₂)₀₋₂N(R^aR^b),
  N(R^a)-C(=O)-(CH₂)₀₋₂N(R^bR^c), -SO₂R^a,
  -N(R^a)SO₂R^b, -SO₂N(R^aR^b), or -N(R^a)-C(R^b)=O,
- (3)  $-NO_2$ ,
- (4) oxo,
- $(5) -C(=O)R^a,$ 
  - (6) -CO₂Ra,
  - (7) -C(=O)N(RaRb),
  - (8)  $-C(=O)-C_{1-4}$  alkyl-N(RaRb),
  - (9) -SRa,
  - (10)  $-S(=O)R^a$ ,
    - (11)  $-SO_2R^a$ ,
    - (12) -N(RaRb),
    - (13) -Rm,
    - (14) -C1-6 alkyl-Rm, wherein the alkyl is optionally substituted with

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		from 1 to 5 substituents each of which is independently
		halogen, -OH, -CN, -C1-4 haloalkyl, -O-C1-4 alkyl,
	,	-O-C ₁₋₄ haloalkyl, -C(=O)Ra, -CO ₂ Ra, -SRa,
		$-S(=O)Ra$ , $-N(RaRb)$ , $-N(Ra)CO_2Rb$ , $-SO_2Ra$ ,
5		$-N(R^a)SO_2R^b$ , $-SO_2N(R^aR^b)$ , or $-N(R^a)-C(R^b)=O$ ,
_	(15)	$-C_{0-4}$ alkyl-N(R ^a )-C ₀₋₄ alkyl-R ^m ,
	(16)	-C ₀₋₄ alkyl-O-C ₀₋₄ alkyl-R ^m ,
	(17)	-C ₀₋₄ alkyl-S-C ₀₋₄ alkyl-R ^m ,
	(18)	-C ₀₋₄ alkyl-C(=0)-C ₀₋₄ alkyl-R ^m ,
10	(19)	$-C(=O)-O-C_{0-4}$ alkyl- $R^{m}$ ,
	(20)	$-C(=O)N(R^a)-C_{0-4}$ alkyl- $R^m$ ,
	(21)	-N(Ra)C(=O)-Rm
	(22)	-N(Ra)C(=O)-C ₁₋₆ alkyl-R ^m , wherein the alkyl is optionally
		substituted with from 1 to 5 substituents each of which
15		is independently halogen, -OH, -CN, -C1-4 haloalkyl,
		$-O-C_{1-4}$ alkyl, $-O-C_{1-4}$ haloalkyl, $-C(=O)R^a$ , $-CO_2R^a$ ,
		$-SRa$ , $-S(=O)Ra$ , $-N(RaRb)$ , $-N(Ra)CO_2Rb$ , $-SO_2Ra$ ,
		$-N(R^a)SO_2R^b$ , $-SO_2N(R^aR^b)$ , or $-N(R^a)-C(R^b)=O$ ,
	(23)	$-N(R^a)-C(=O)-N(R^b)-C_0-4$ alkyl $-R^m$ ,
20	(24)	$-N(R^a)-C(=O)-O-C_{0-4}$ alkyl- $R^m$ , or
	(25)	$-N(R^a)-C(=O)-N(R^b)SO_2-C_0-4$ alkyl- $R^m$ ;
	wherein each Rm is	independently aryl selected from phenyl and naphthyl; a 5- or 6-
	membered saturated	heterocyclic ring containing from 1 to 3 heteroatoms
25	independently select	ed from N, O and S; a 5- or 6-membered heteroaromatic ring
	containing from 1 to	3 heteroatoms independently selected from N, O and S; or a 9- to
	10-membered bicycl	ic heterocycle which is saturated or unsaturated and contains
	from 1 to 3 heteroate	oms independently selected from N, O and S; wherein
		and the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of the state of t

-N(RaRb); the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C₁₋₄ alkyl or oxo, and is additionally optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-(CH₂)₁₋₂-phenyl; and

which is independently halogen, -C1_4 alkyl, -CF3, -O-C1_4 alkyl, -OCF3, or

the aryl is optionally substituted with from 1 to 3 substituents each of

the heteroaromatic ring or the bicyclic heterocycle is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl or oxo;

- 5 or a pharmaceutically acceptable salt thereof.
  - 31. The compound according to claim 30, wherein

R1 is:

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$$R^8$$
,  $R^8$ , or  $R^8$ 

R⁸ is:

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- (1) -H,
- -C1-4 alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C1-4 alkyl, -OCF3, -C(=O)Ra, -CO₂Ra, -SRa, -N(RaRb), or -C(=O)N(RaRb),

- (3)  $-C(=O)R^a$ ,
- (4) -CO₂Ra,

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-C(=O)-(CH_2)_{1-2}-N(R^aR^b),
                        (5)
                                 -SO<sub>2</sub>Ra,
                        (6)
                                 -(CH_2)_{1-2}-R^m,
                        (7)
                                 -(CH<sub>2</sub>)<sub>0-2</sub>-C(=O)-(CH<sub>2</sub>)<sub>0-2</sub>-R<sup>m</sup>,
                        (8)
                                 -C(=O)-O-(CH_2)_{0-2}-R^m, or
                        (9)
 5
                                 -C(=O)N(R^a)-(CH_2)_{0-2}-R^m;
                        (10)
       R9 is -H, -C<sub>1-4</sub> alkyl, or oxo;
      R^{10} is -H, -OH, -C1-4 alkyl, -O-C1-4 alkyl, oxo, or -O-(CH2)1-2-Rm;
10
       R11 is
                        (1)
                                 -H,
                                 -C<sub>1-4</sub> alkyl, which is optionally substituted with 1 or 2
                        (2)
                                 substituents each of which is independently -OH, -O-C1-4
15
                                 alkyl, -OCF3, -C(=O)Ra, -CO2Ra, -SRa, -N(RaRb), or
                                 -C(=O)N(RaRb),
                                 -C(=O)Ra
                         (3)
                                 -CO2Ra,
                         (4)
                                 -C(=O)-(CH_2)_{1-2}-N(R^aR^b),
                         (5)
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                                 -SO<sub>2</sub>Ra,
                         (6)
                                 -(CH_2)_{1-2}-R^m,
                         (7)
                                 -(CH_2)_{0-2}-C(=O)-(CH_2)_{0-2}-R^m
                         (8)
                                 -C(=O)-O-(CH_2)_{0-2}-R^m, or
                         (9)
                                 -C(=O)N(Ra)-(CH_2)_{0-2}-Rm;
25
                         (10)
       with the proviso that when one of R^8 and R^{11} is -(CH<sub>2</sub>)<sub>1-2</sub>-R^m,
```

-(CH₂)₀₋₂-C(=O)-(CH₂)₀₋₂-R^m, -C(=O)-O-(CH₂)₀₋₂-R^m, or -C(=O)N(R^a)-(CH₂)₀₋₂-R^m, then the other of R⁸ and R¹¹ is other than -(CH₂)₁₋₂-R^m, -(CH₂)₀₋₂-C(=O)-(CH₂)₀₋₂-R^m, -C(=O)-O-(CH₂)₀₋₂-R^m, or -C(=O)N(R^a)-(CH₂)₀₋₂-R^m;

Rm is aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated heterocyclic ring containing 1 or 2 heteroatoms independently selected from N and O;

a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a saturated or unsaturated heterocycle containing from 1 to 3 nitrogen atoms; wherein

the aryl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, or -N(RaRb); and

the saturated heterocyclic ring is optionally substituted with from 1 to 3 substituents each of which is independently -C₁₋₄ alkyl or oxo; and is additionally and optionally mono-substituted with phenyl, -(CH₂)₁₋₂-phenyl, -C(=O)-phenyl, -CO₂-phenyl, or -CO₂-(CH₂)₁₋₂-phenyl; and

the heteroaromatic ring or the bicyclic heterocycle is optionally substituted with 1 or 2 substituents each of which is independently -C₁₋₄ alkyl or oxo; and

each Ra and Rb is independently -H or -C1_4 alkyl;

or a pharmaceutically acceptable salt thereof.

32. The compound according to claim 31, wherein

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R² is -H or methyl;

R³ is -H; and

25 R⁴ is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, -CN, or -SO₂R^a; and is additionally and optionally monosubstituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

30

or a pharmaceutically acceptable salt thereof.

33. The compound according to claim 1, which is a compound of Formula (II):

$$\mathbb{R}^{12}$$
  $\mathbb{N}$   $\mathbb{N}$   $\mathbb{N}$   $\mathbb{N}$   $\mathbb{N}^3$   $\mathbb{N}$   $\mathbb{N}^4$   $\mathbb{N}$   $\mathbb{N}^4$   $\mathbb{N}$   $\mathbb{N}$ 

wherein T is:

(14)

(15)

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-H, (1) -OH. **(2)** -C₁₋₄ haloalkyl, (3) - $C_{1-3}$  alkyl, optionally substituted with -OH or -O- $C_{1-4}$  alkyl, (4) -O-C₁₋₄ haloalkyl, (5) -O-C₁₋₄ alkyl (6) -N(RaRb),(7) -N(Ra)-(CH2)2-OH, (8)  $-N(Ra)-CO_2R^b$ , (9)  $-N(R^a)-C(=O)-(CH_2)_{1-2}-N(R^aR^b),$ (10)-Rk, (11)-(CH2)1-4-RK, (12)-(CH₂)₀₋₂-O-(CH₂)₀₋₂-R^k, (13)

Rk is aryl selected from phenyl and naphthyl; a 5- or 6-membered saturated 20 heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S; wherein 25

 $-(CH_2)_{0-2}-N(R^a)-(CH_2)_{0-3}-R^k$ , or

-(CH₂)₀₋₂-N(Ra)-C(=O)-(CH₂)₀₋₂-R^k;

the aryl is optionally substituted with from 1 to 4 substituents each of which is independently halogen, -C1-4 alkyl, -C1-4 alkyl-ORa, -C1-4

haloalkyl, -O-C1-4 alkyl, -O-C1-4 haloalkyl, or -N(RaRb); and

the saturated heterocyclic ring is optionally substituted with from 1 to 4 substituents each of which is independently -C1-4 alkyl; -C1-4 alkyl-ORa;

-C₁₋₄ haloalkyl; -O-C₁₋₄ alkyl; -O-C₁₋₄ haloalkyl; -C(=O)R^a; oxo; ethylenedioxy spiro substituted on a ring carbon; phenyl; -CH₂-phenyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; -CH₂-saturated heterocycle which is a a 5- or 6-membered ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S;

the heteroaromatic ring is optionally substituted with from 1 to 4 substituents each of which is independently -C₁₋₄ alkyl, -C₁₋₄ alkyl-OR^a, -C₁₋₄ haloalkyl, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, or oxo; and

the bicyclic heterocycle is optionally substituted with from 1 to 4 substituents each of which is independently -C₁₋₄ alkyl or oxo;

R12 is phenyl which is optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, Br, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, methylenedioxy attached to two adjacent carbon atoms, or phenyl;

each Ra and Rb is independently -H or -C1-4 alkyl; and

s is an integer equal to zero, 1, 2, or 3;

or a pharmaceutically acceptable salt thereof.

34. The compound according to claim 33, wherein

R³ is -H; and

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R⁴ is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, -CN, -SR^a, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

or a pharmaceutically acceptable salt thereof.

35. The compound according to claim 33, wherein

s is zero, 1 or 2;

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and with the proviso that when s is 1 or 2, T is -H;

or a pharmaceutically acceptable salt thereof.

Formula (III):

wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, -CN, -SRa, or -SO₂Ra; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

or a pharmaceutically acceptable salt thereof.

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37. The compound according to claim 1, wherein

R¹ is

1/~ 1/

(1) -C₁₋₄ alkyl, which is optionally substituted with 1 to 3 substituents each of which is independently fluoro, chloro, -OH, -O-C₁₋₄ alkyl, -O-C₁₋₄ haloalkyl, -C(=O)R^a, -CO₂R^a, -SR^a, -S(=O)R^a, -N(R^aR^b), -C(=O)-(CH₂)₀₋₂N(R^aR^b),

-N(Ra)-C(=O)-(CH2)1-2N(RbRc), -SO2Ra, -N(Ra)SO2Rb,

 $-SO_2N(RaRb)$ , -N(Ra)-C(Rb)=O,

 $-N(R^a)C(=O)N(R^bR^c)$ ,  $-N(R^a)C(=O)C(=O)N(R^bR^c)$ , or

-N(Ra)C(=O)ORb,

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- (2)  $-(CH_2)_{1-3}-R^k$ ,
- (3)  $-(CH_2)_{1-3}-O-(CH_2)_{0-2}-R^k$ ,
- (4)  $-(CH_2)_{1-3}-N-(CH_2)_{0-2}-R^k$ ,
- (5)  $-(CH_2)_{1-3}-N(R_a)C(=O)-(CH_2)_{0-2}-R^k$ ,
- (6)  $-(CH_2)_{1-3}-N(R^a)C(=O)-O-(CH_2)_{0-2}-R^k$ ,

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- (7)  $-(CH_2)_{0-3}-C(=O)N(R^a)-(CH_2)_{0-2}-R^k$ , or
- (8)  $-C(=O)-(CH_2)_{0-2}-R^k$ ,
- (9)  $-C(CH_3)_2N(R_a)C(=O)OCH_2R^k$ ,
- (10)  $-C(CH_3)_2N(R_a)CH_2R_k$ ,
- (11)  $-C(CH_3)_2N(R_a)C(=O)R^k$ ,
- 15
- (12)  $-C(R^b)(N(R^a)C(=O)R^k)(CH_2OR^c)$ , or
- (13)  $-C(R^b)(N(R^a)(CH_2)-R^k)(CH_2OR^c),$

Rk is aryl selected from phenyl and naphthyl, with the proviso that when R¹ is -(CH₂)₁₋₃-Rk, then Rk is not phenyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S, with the proviso that the bicyclic heterocycle is not benzo-1,3-dioxolyl;

wherein the aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

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- (1) fluoro, chloro, or bromo,
- (2) -OH,
- (3) -CN,

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	(4) (4)	-CF3, -C ₁₋₄ alkyl, which is optionally substituted with 1 or 2 substituents each of which is independently -OH, -O-C ₁₋₄ alkyl, -OCF ₃ , -C(=O)R ^a , -CO ₂ R ^a , -SR ^a , or -N(R ^a R ^b ),
5	(5) (5)	-OCF ₃ , -O-C ₁₋₄ alkyl,
10	(8) (9) (10) (11)	oxo, methylenedioxy attached to two adjacent ring carbon atoms, $-C(=O)R^a$ , $-CO_2R^a$ ,
	(12) (13) (14)	-SRa, -S(=O)Ra, -N(RaRb), -(CH ₂ ) ₀₋₂ -C(=O)N(RaRb),
15	(16)	-C(=O)-(CH ₂ ) ₁₋₂ -N(RaRb), or -SO ₂ Ra;

or a pharmaceutically acceptable salt thereof.

38. The compound according to claim 37, wherein

R² is -H; and

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R⁴ is -CH₂-Q; wherein Q is phenyl optionally substituted with from 1 to 3

substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃,
-O-C₁-4 alkyl, -OCF₃, -CN, or -SO₂R^a; and is additionally and optionally monosubstituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

30 each Ra and Rb is independently -H or -C1-4 alkyl;

 $R^k$  is aryl selected from phenyl and naphthyl, with the proviso that when  $R^1$  is -(CH₂)₁₋₃- $R^k$ , then  $R^k$  is not phenyl; a bicyclic carbocycle selected from indanyl and tetrahydronaphthyl; a 5- or 6-membered saturated heterocyclic ring containing from 1

to 4 heteroatoms independently selected from N, O and S; a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S; or a bicyclic heterocycle which is a benzene ring fused to a 5- or 6-membered saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from N, O and S, with the proviso that the bicyclic heterocycle is not benzo-1,3-dioxolyl;

wherein the aryl, bicyclic carbocycle, saturated heterocyclic ring, heteroaromatic ring, or bicyclic heterocycle is optionally substituted with from 1 to 3 substituents each of which is independently

fluoro, chloro, or bromo, 10 (1) **(2)** -OH, -CN, (3) (4) -CF3, -C₁₋₄ alkyl, which is optionally substituted with 1 or 2 (4) substituents each of which is independently -OH, -O-C1-4 15 alkyl, -OCF3, -C(=O)Ra, -CO2Ra, -SRa, or -N(RaRb), -OCF3, **(5)** -O-C₁₋₄ alkyl, (5) (8) oxo, methylenedioxy attached to two adjacent ring carbon atoms, 20 (9)  $-C(=O)R^a$ , (10)-CO2Ra, (11)-SRa, (12)-S(=O)Ra, (13)-N(RaRb),25 (14)  $-(CH_2)_{0-2}-C(=O)N(R^aR^b),$ (15) $-C(=O)-(CH_2)_{1-2}-N(R^aR^b)$ , or (16)(17) -SO₂Ra;

- or a pharmaceutically acceptable salt thereof.
  - 39. The compound according to claim 1, which is a compound of Formula (IV):

wherein Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁-4 alkyl, -CF₃, -O-C₁-4 alkyl, -OCF₃, -CN, -SR^a, or -SO₂R^a; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

or a pharmaceutically acceptable salt thereof.

10 40. The compound according to claim 1, which is a compound of Formula (V):

wherein

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R13 is -H or -C1-6 alkyl;

R¹⁴ is -H, -C₁₋₆ alkyl, -C(=O)-C₁₋₆ alkyl, -C(=O)-(CH₂)₀₋₂-J, or
-C(=O)-O-(CH₂)₀₋₂-J; wherein J is aryl selected from phenyl and naphthyl; a 5- or
6-membered saturated heterocyclic ring containing from 1 to 4 heteroatoms
independently selected from N, O and S; or a 5- or 6-membered heteroaromatic ring
containing from 1 to 4 heteroatoms independently selected from N, O and S; and

wherein the aryl is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, chloro, bromo, -CF3, -C1-4 alkyl, -OCF3, or -O-C1-4 alkyl; and

wherein the saturated heterocyclic ring or heteroaromatic ring is optionally substituted with from 1 to 3 substituents each of which is independently fluoro, chloro, bromo, -CF3, -C1-4 alkyl, -OCF3, -O-C1-4 alkyl, or oxo;

R15 and R16 are each independently -C1-6 alkyl; or alternatively R15 and R16 together with the carbon atom to which they are both attached form C3-8 cycloalkyl; and

Q is phenyl optionally substituted with from 1 to 3 substituents each of which is independently -F, -Cl, -Br, -OH, -C₁₋₄ alkyl, -CF₃, -O-C₁₋₄ alkyl, -OCF₃, -CN, -SRa, or -SO₂Ra; and is additionally and optionally mono-substituted with methylenedioxy attached to two adjacent ring carbon atoms, phenyl, or -O-phenyl;

or a pharmaceutically acceptable salt thereof.

41. The compound according to claim 40, wherein

R15 and R16 are both methyl; or alternatively R15 and R16 together with the carbon atom to which they are both attached form cyclohexyl;

- or a pharmaceutically acceptable salt thereof.
  - 42. A compound according to claim 1, which is a compound selected from the group consisting of
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-1-(methylamino)ethyl]pyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylmorpholin-3-yl)pyrimidine-4-carboxamide;

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- 2-[1-benzoyl-4-(N,N-dimethylglycyl)piperazin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(1-benzoyl-4-methylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpiperidin-2-yl)pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)-1,2,3,4-tetrahydroquinolin-2-yl]pyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[4-methyl-1-(pyridin-2-ylcarbonyl)piperazin-2-yl]pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-4-(pyridin-2-ylcarbonyl)piperazin-2-yl]pyrimidine-4-carboxamide;
- 2-(1-ethylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-20 carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-isopropyl-1-methylpiperazin-2-yl)pyrimidine-4-carboxamide;
- 25 2-[1-(acetylamino)cyclohexyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluor obenzyl)-5, 6-dihydroxy-2-[1-(morpholin-4-ylacetyl)piperidin-2-yl]pyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(pyrrolidin-1-ylmethyl)pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpyrrolidin-2-yl)pyrimidine-4-35 carboxamide;

- 2-[1-(N,N-dimethylglycyl)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 5 N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[(pyridin-2-lcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
  - 2-[1-(dimethylamino)-2-phenylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-{1-[(2,4-dimethyl-1,3-thiazol-5-yl)carbonyl]piperidin-2-yl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(3-chlorobenzoyl)-4-methylpiperazin-2-yl]-N-(4-fluorobenzyl)-5,6dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-4-(methylsulfonyl)piperazin-2-yl]pyrimidine-4-carboxamide;
- 20 N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-isopropyl-4-methylpiperazin-2-yl)pyrimidine-4-carboxamide;
  - N-(3-bromo-4-fluorobenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-[1-(dimethylamino)cyclohexyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-[(pyridin-2-30 ylcarbonyl)amino]cyclohexyl}pyrimidine-4-carboxamide;
  - 2-(4-benzyl-1-methylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(1-piperidin-1-ylethyl)phenyl]pyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(2-methyl-1,2,3,4-tetrahydroisoquinolin-3-yl)pyrimidine-4-carboxamide;
  - N-(2,3-dimethoxybenzyl)-2-[1-(N,N-dimethylglycyl)piperidin-2-yl]-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(anilinocarbonyl)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-[(2S,4R)-1-benzoyl-4-(benzyloxy)pyrrolidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)piperidin-2-yl]pyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-(morpholin-4-ylacetyl)-1,2,3,4-20 tetrahydroisoquinolin-3-yl]pyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-phenyl-1-[(pyridin-2-lcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;

- 25 2-(1-benzoylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-(1-benzylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-(1-benzoylpyrrolidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-isonicotinoylpiperidin-2-yl)pyrimidine-4-35 carboxamide;

- N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-(1-isonicotinoylpiperidin-2-yl)pyrimidine-4-carboxamide;
- 5 N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(methylsulfonyl)piperidin-2-yl]pyrimidine-4-carboxamide;
  - 2-(1-benzoyl-1,2,3,4-tetrahydroquinolin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

2-{1-[(N,N-dimethylglycyl)amino]-2-phenylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

- N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(piperidin-1-ylmethyl)phenyl]pyrimidine-4-carboxamide;
  - 2-{4-[(diethylamino)methyl]phenyl}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-4-ylmethyl)piperidin-2-yl]pyrimidine-4-carboxamide;
  - 2-(1-benzoylpyrrolidin-2-yl)-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

tert-butyl 2-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)morpholine-4-carboxylate;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-3-ylcarbonyl)piperidin-2-30 yl]pyrimidine-4-carboxamide;
  - 2-[2-(N,N-dimethylglycyl)-1,2,3,4-tetrahydroisoquinolin-3-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

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- 2-(1-benzoyl-2,3-dihydro-1H-indol-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(2-benzoyl-1,2,3,4-tetrahydroisoquinolin-3-yl)-N-(4-fluorobenzyl)-5,6-5 dihydroxypyrimidine-4-carboxamide;
  - 2-(1-amino-2-phenylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-(4-benzylmorpholin-3-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-[(1-methyl-1H-imidazol-2-yl)carbonyl]piperidin-2-yl}pyrimidine-4-carboxamide;
- N-(2,3-dimethoxybenzyl)-5,6-dihydroxy-2-[4-(morpholin-4-ylmethyl)phenyl]pyrimidine-4-carboxamide;
- *N*-(4-fluorobenzyl)-5,6-dihydroxy-2-(morpholin-4-ylmethyl)pyrimidine-4-20 carboxamide;
  - N-(4-Fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-{4-[({[(2-chlorophenyl)sulfonyl]amino}carbonyl)amino]thien-3-yl}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4 carboxamide;
  - $N^4$ -(4-fluorobenzyl)-5,6-dihydroxy- $N^2$ -(pyridin-2-ylmethyl)pyrimidine-2,4-dicarboxamide;
- 30 2-Benzyl-*N*-(4-fluorobenzyl)-5-hydroxy-6-(2-morpholin-4-ylethoxy)pyrimidine-4-carboxamide;
  - and pharmaceutically acceptable salts thereof.

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	43.	A compound accord	rding to claim	42,	which is	a compound
selected from	the gro	up consisting of				

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methylpiperidin-2-yl)pyrimidine-4-carboxamide;
  - 2-[1-(dimethylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 10 N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylmorpholin-3-yl)pyrimidine-4carboxamide;
  - 2-[(dimethylamino)(phenyl)methyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-{4-[(diethylamino)methyl]phenyl}-N-(2,3-dimethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
    - N-benzyl-5, 6-dihydroxy-2-(3-phenyl propyl) pyrimidine-4-carbox amide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-(pyridin-2-ylcarbonyl)-1,2,3,4-tetrahydroquinolin-2-yl]pyrimidine-4-carboxamide;
    - and pharmaceutically acceptable salts thereof.
    - 44. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
- 30 45. A method of inhibiting HIV integrase in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

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46. A method for preventing or treating infection by HIV or for preventing, treating or delaying the onset of AIDS in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

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- 47. The method according to claim 46, wherein the compound is administered in combination with a therapeutically effective amount of at least one antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors and nucleoside HIV reverse transcriptase inhibitors.
- 48. A pharmaceutical composition which comprises the product prepared by combining an effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

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- 49. A combination useful for inhibiting HIV integrase, for treating or preventing infection by HIV, or for preventing, treating or delaying the onset of AIDS, which is a therapeutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a therapeutically effective amount of an HIV infection/AIDS antiviral agent selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors and nucleoside HIV reverse transcriptase inhibitors.
- 50. A compound according to claim 1, which is a compound selected from the group consisting of
  - benzyl 1-[4-({[4-fluoro-2-(methylsulfonyl)benzyl]amino}carbonyl)-5,6-dihydroxypyrimidin-2-yl]-1-methylethylcarbamate;
- 30 2-(1-amino-1-methylethyl)-N-[4-fluoro-2-(methylsulfonyl)benzyl]-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-[1-(dimethylamino)-1-methylethyl]-N-[4-fluoro-2-(methylsulfonyl)benzyl]-5,6-dihydroxypyrimidine-4-carboxamide;

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- 2-(1-aminocyclopropyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(dimethylamino)cyclopropyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-[(pyrazin-2-ylcarbonyl)amino]cyclopropyl}pyrimidine-4-carboxamide;

benzyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)cyclopentylcarbamate;

- 2-(1-aminocyclopentyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(dimethylamino)cyclopentyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4carboxamide;
  - 2-(1-{[(ethylamino)carbonyl]amino}-1-methylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 20 2-[1-(benzylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-[1-(benzoylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-{1-[benzyl(methyl)amino]-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(dimethylamino)-1-methylethyl]-N-(2-ethoxybenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(2-chlorobenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;

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N-(2-chlorobenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;

N-(5-chloro-2-methylbenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-5 dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[(pyrazin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;

2-[1-(diethylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-morpholin-4-ylethyl)pyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-piperidin-1-ylethyl)pyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-pyrrolidin-1-ylethyl)pyrimidine-4-20 carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[methyl(pyridin-4-ylmethyl)amino]ethyl}pyrimidine-4-carboxamide;

25 2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxy-N-[2-(methylthio)benzyl]pyrimidine-4-carboxamide;

N1,N1-diethyl- $N\sim2\sim-[1-(4-\{[(4-fluorobenzyl)amino]carbonyl\}-5,6-dihydroxypyrimidin-2-yl)-1-methylethyl]ethanediamide;$ 

2-[1-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1-methyl-1-{[(1-methyl-1H-imidazol-2-yl)carbonyl]amino}ethyl)pyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[1-methyl-1-(4-oxopiperidin-1-yl)ethyl]pyrimidine-4-carboxamide;
- 5 N-(4-fluorobenzyl)-5,6-dihydroxy-2-{1-methyl-1-[methyl(pyridin-2-ylmethyl)amino]ethyl}pyrimidine-4-carboxamide;
  - N-[1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-1-methylethyl]-4-methylmorpholine-2-carboxamide;
- 10
  2-{1-[acetyl(methyl)amino]-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(acetylamino)-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-{1-[4-(dimethylamino)piperidin-1-yl]-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 20 N-(2,3-dimethoxybenzyl)-2-[1-(dimethylamino)-1-methylethyl]-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-[4-(dimethylamino)tetrahydro-2H-pyran-4-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(7-methyl-7-azabicyclo[2.2.1]hept-1-yl)pyrimidine-4-carboxamide;
- 2-(7-acetyl-7-azabicyclo[2.2.1]hept-1-yl)-N-(4-fluorobenzyl)-5,6-30 dihydroxypyrimidine-4-carboxamide;
  - 2-(2-acetyl-2-azabicyclo[2.1.1]hex-1-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-(2-methyl-2-azabicyclo[2.1.1]hex-1-yl)pyrimidine-4-carboxamide;

- tert-butyl (2S,4R)-4-(benzyloxy)-2-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)piperidine-1-carboxylate;
  - 2-[(2S,4R)-4-(benzyloxy)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[(2S,4R)-4-(benzyloxy)-1-methylpiperidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(2S,4R)-4-hydroxy-1-methylpiperidin-2-yl]pyrimidine-4-carboxamide;
- 15
  2-[1-acetyl-4-(benzyloxy)piperidin-2-yl]-N-(4-fluorobenzyl)-5,6dihydroxypyrimidine-4-carboxamide;
- 2-(1-ethyl-4-methylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[4-methyl-1-(pyrazin-2-ylcarbonyl)piperazin-2-yl]pyrimidine-4-carboxamide;
- 25 tert-butyl 3-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)thiomorpholine-4-carboxylate;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-thiomorpholin-3-ylpyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(4-methylthiomorpholin-3-yl)pyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[4-(pyridin-2-ylcarbonyl)thiomorpholin-3-yl]pyrimidine-4-carboxamide;

- 2-(4-acetylthiomorpholin-3-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- tert-butyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-2-methoxyethylcarbamate;
  - 2-[1-(dimethylamino)-2-methoxyethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-[1-(acetylamino)-2-methoxyethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-(1-amino-2-methoxyethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;

N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-[(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-2-[1-(formylamino)-2-methoxyethyl]-5,6-dihydroxypyrimidine-4-20 carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methoxy-1-(methylamino)ethyl]pyrimidine-4-carboxamide;
- 25 2-{1-[acetyl(methyl)amino]-2-methoxyethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-[methyl(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(4R)-3-(pyridin-2-ylcarbonyl)-1,3-thiazolidin-4-yl]pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(4R)-1,3-thiazolidin-4-yl]pyrimidine-4-35 .carboxamide;

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N-(4-fluorobenzyl)-5,6-dihydroxy-2-[(4R)-3-methyl-1,3-thiazolidin-4-yl]pyrimidine-4-carboxamide;

- 5 2-(3-acetyl-1,3-thiazolidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-(3-methyl-1,3-thiazolidin-2-yl)pyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-(1,2,4-trimethylpiperazin-2-yl)pyrimidine-4-carboxamide;
- 2-[2,4-dimethyl-1-(pyrazin-2-ylcarbonyl)piperazin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-(1-acetyl-2,4-dimethylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- tert-butyl 1-(4-{[(4-fluorobenzyl)amino]carbonyl}-5,6-dihydroxypyrimidin-2-yl)-2-methoxy-1-methylethylcarbamate;
  - 2-(1-amino-2-methoxy-1-methylethyl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - $\hbox{$2$-[1-(acetylamino)-2-methoxy-1-methylethyl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;}$
- 2-[1-(dimethylamino)-2-methoxy-1-methylethyl]-N-(4-fluorobenzyl)-5,6-30 dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methoxy-1-methyl-1-(methylamino)ethyl]pyrimidine-4-carboxamide;

- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-methyl-1-[(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
- 2-(1,2-dimethylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4carboxamide;
  - 2-{1-[acetyl(methyl)amino]-2-methoxy-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-{2-methoxy-1-methyl-1-[methyl(pyridin-2-ylcarbonyl)amino]ethyl}pyrimidine-4-carboxamide;
  - $2-\{1-[(cyclohexylmethyl)(methyl)amino]-2-methoxy-1-methylethyl\}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;$
  - 2-{1-[(cyclohexylmethyl)amino]-2-methoxy-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 2-{1-[(cyclohexylmethyl)amino]-2-methoxy-1-methylethyl}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - 2-(4-acetyl-1,2-dimethylpiperazin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
- 25 2-(1-acetyl-2-methylpiperidin-2-yl)-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methyl-1-(pyrazin-2-ylcarbonyl)piperidin-2-yl]pyrimidine-4-carboxamide;
  - N-(2,3-dimethoxybenzyl)-2-(1,2-dimethylpiperidin-2-yl)-5,6-dihydroxypyrimidine-4-carboxamide;
- N-(4-fluorobenzyl)-5,6-dihydroxy-2-[2-methyl-1-(pyridin-2-ylcarbonyl)piperidin-2-yl]pyrimidine-4-carboxamide;

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 $2-\{1-[(2,4-dimethyl-1,3-thiazol-5-yl)carbonyl]-2-methylpiperidin-2-yl\}-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;$ 

- 5 2-[(2S)-1-acetyl-2-methylpyrrolidin-2-yl]-N-(4-fluorobenzyl)-5,6-dihydroxypyrimidine-4-carboxamide;
  - and pharmaceutically acceptable salts thereof.

#### INTERNATIONAL SEARCH REPORT

Interna Application No

PCT/GB 02/04742 A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/513 A61K C07D239/557 A61K31/541 C07D239/52 A61K31/5377 C07D401/12 C07D401/14 C07D403/04 C07D401/04 C07D401/06 CO7D403/12 C07D403/14 CO7D405/04 C07D413/04 C07D409/04 According to international Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K C07D Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) CHEM ABS Data, WPI Data, EPO-Internal C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Calegory ' Citation of document, with indication, where appropriate, of the relevant passages WO 01 00578 A (EGBERTSON MELISSA S ;FISHER 1 - 50THORSTEN E (US); MELAMED JEFFREY Y (US) 4 January 2001 (2001-01-04) * the entire document * 1 - 50A WO 99 62520 A (EGBERTSON MELISSA ; FISHER THORSTEN E (US); CLARK DAVID L (US); EMB)
9 December 1999 (1999-12-09) cited in the application * the entire document * 1 - 50US 6 306 891 B1 (EGBERTSON MELISSA ET AL) 23 October 2001 (2001-10-23) * the entire document * Patent family members are listed in annex. X Further documents are listed in the continuation of box C. Special categories of cited documents: T later document published after the international filling date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the 'A' document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the International "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docucitation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means document published prior to the International filing date but later than the priority date claimed *&* document member of the same patent family Date of the actual completion of the international search Date of mailing of the International search report 28/01/2003 15 January 2003 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patenthaan 2 NL – 2280 HV Rijswijk Tet. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

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## INTERNATIONAL SEARCH REPORT

onal application No. PCT/GB 02/04742

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  Although claims 45-47 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
Claims Nos.:     because they relate to parts of the International Application that do not comply with the prescribed requirements to such because they relate to parts of the International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:  1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all
As all required additional section loss that a state of searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

### INTERNATIONAL SEARCH REPORT

mazmation on patent family members

Interna Application No
PCT/GB 02/04742

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